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BRITISH MEDICAL BULLETIN

Part I: Industrial Hazards

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TOXICOLOGICAL HAZARDS: NON-METALS
TOXIC INDUSTRIAL SOLVENTS
HAZARDS FROM INSECTICIDES
OCCUPATIONAL SKIN DISEASE
COALMINERS' PNEUMOCONIOSIS
SILICOSIS AND OTHER PNEUMOCONIOSES
BYSSINOSIS IN THE COTTON INDUSTRY
RADIATION HAZARDS
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BRITISH MEDICAL BULLETIN
VOLUME 7 NUMBER 1–2 1950

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Industrial Hazards

The first half of this century has witnessed an immense expansion of scientific knowledge. Each new discovery has been scrutinized by industry for a possible industrial application. Successful applications have been frequent, and the advance of science has revolutionized techniques over a wide range of industrial processes. Change has usually involved increased complexity. So it is that industry today presents a great variety of health hazards. Since the pioneering work of Legge in Great Britain, much progress has been made in industrial health in this country. Many notorious hazards of the recent past have been largely overcome, but new hazards have arisen to take their place.

The papers which make up this symposium deal with all the major health hazards of modern industry. It is unlikely that the doctor who spends all or part of his time in industry will encounter the majority of the hazards described here in his own practice. It must be admitted, however, that industrial disease has often been detected too late ; this should not happen if a wide knowledge of the possibilities is combined with careful observation.

This symposium exposes the fallacy of dividing the practice of medicine into two compartments, preventive and clinical. Occupational disease is a *clinical* entity. To deal with it effectively, the doctor in industry must have a sound training in clinical medicine. Yet the discovery of a case of occupational disease imposes an obligation on the doctor in industry to prevent the development of other cases. Here is an exercise in preventive medicine. The doctor in industry is in a unique and happy position, for he has the opportunity, denied to most of his fellows, to practise clinical and preventive medicine as they should be practised, together.

Implicit in many of the papers which follow this introduction is the idea that a national industrial health service would do much to improve the health of the working population. Clearly such a unified service would represent an immense advance in the provision of health services in Great Britain. Were it possible to effect a rational integration of the hospital and public health services a national industrial health service would fall naturally into place.

From a study of this symposium, it will be evident that great advances have been made in recent years in the identification, elucidation and prevention of industrial health hazards. New hazards are constantly arising, however, and there can be no relaxation in research. It may be noted that of the sixteen contributors to this symposium, ten are members of the scientific staff of the Medical Research Council. Since the days of the First World War, the Medical Research Council has played a predominant part in industrial health research in this country. This is, no doubt, as it should be, in so far as fundamental research is concerned. But the prevention of industrial health hazards can be largely assisted by applied or operational research, which is necessary as a complement of fundamental research if the best results are to be obtained. Ideal opportunities exist for applied research in industry, and it is to be hoped that industry will shoulder an increasing responsibility for the prosecution of this type of research.

The first group of papers is concerned with different aspects of toxicology. Hunter discusses the toxicology of metals which have found new uses in industry, or which have been used increasingly in recent years. The pathological syndromes caused by these metals, which until a few years ago were scientific curiosities, are now reasonably well known. In the majority of instances, however, their exact mode of action in the body remains a mystery. The toxicology of the organic compounds of silicon and fluorine, comparative new-comers to industry of which much more will be heard, is described by Taylor. Browning reviews some of the aromatic and cyclic hydrocarbons. Her warning that familiarity with well-known poisons, such as benzene, may lead to contempt and so to disaster, should be heeded.

Barnes in his paper on insecticides raises a problem of growing importance—the effects on man of prolonged ingestion of foods contaminated by the synthetic insecticides which are now flooding the world's markets. The acute effects of these insecticides on mammals can be ascertained without much difficulty, and are sometimes insignificant, but their chronic effects remain quite unknown. A rational solution of this problem must await expansion of the national resources for research in toxicology. Lest these resources be overtaxed by the long-term examination of a multiplicity of synthetic chemicals, some screening organization will be needed to decide on priorities and on the exclusion of compounds for the use of which there is no clear indication or need. It is also highly desirable that research on the metabolism of the Insecta should be energetically pursued so that new insecticides may be developed on a scientific rather than on an empirical basis.

The more important occupational diseases are surveyed in the next group of papers. Squire, Cruickshank and Topley contribute a detailed study of occupational skin disease. Their use of statistical method to isolate and define the component parts of the problem is worthy of wider emulation. Another practical lesson may be learnt from their undramatic but none the less important statement that by far the greatest amount of time lost in industry due to occupational skin disease can be attributed to substances which are generally recognized as potentially harmful, and that consequently a closer study of the methods of using these agents might result in a considerable reduction of the problem of dermatitis.

Fletcher and Gough, in their communication on coalminers' pneumoconiosis, make it clear that though solid progress has been achieved in the study of this disease, old-standing problems of etiology remain unsolved. Discussions on research on coalminers' pneumoconiosis are frequently enlivened by controversy about the relative values of laboratory work and environmental studies. It is probably true that both methods of approach are essential if final and convincing conclusions are to be reached. Middleton, with the authority of long experience, surveys silicosis and the other pneumoconioses. It is apparent from this and the foregoing paper that the pneumoconioses are still taking a considerable toll of life and health. The therapy of the pneumoconioses remains disappointing and virtually no advance can be recorded. The advent of adrenocorticotropic hormone (ACTH) and cortisone, with their well-established actions on pathological aggregations of fibrous tissue, may change this gloomy picture. Until sufficient quantities of these substances are available for adequate clinical trials the greatest reserve should be exercised in speculating on any beneficial effects they might exert in this group of diseases. Early reports on cortisone suggest that its action in tuberculosis is unfavourable, and tuberculosis

is commonly associated with the pneumoconioses. Schilling's paper, which gives a full account of byssinosis, suggests that mortality from this disease has been underestimated in the past.

It is appropriate that this symposium, issued at the threshold of the atomic age, should contain an account of radiation hazards in industry, by Edson, and a review of treatment of the radiation syndrome, by Loutit. If all goes well in the ensuing years a rapid increase in the industrial use of atomic energy is to be expected : if the worst befall, masses of the population may be exposed to radiant energy in varying degree. In either case much should be gained by the study of these two very important papers. In considering the dangers of atomic energy in general and of the atomic bomb in particular, it is highly desirable to retain a sense of perspective. It is permissible, therefore, to emphasize Loutit's statement that the vast majority of deaths caused by atomic bombs in Japan were due to multiple causes of which, however, trauma, burns and radiation syndrome, *in that order*, were the most important. The reader may find himself somewhat at a loss to decide on the value of the many treatments advocated for the different stages of the radiation syndrome. *Quot homines, tot sententiae.* Until further fundamental research discloses more about the basic metabolic changes associated with the radiation syndrome it seems that in the mean time reliance should be placed mainly on blood transfusion and the antibiotics.

The last group of papers deals with injuries, accidents and the prevention of sepsis in industry. Bull, who writes on industrial accidents, has made a careful analysis of accidents in the Birmingham area. His paper should be of interest to medical officers working in industries with a high accident rate. Whitfield, in his study on the causes of accidents, emphasizes the value of systematic records of all the relevant circumstances. Subsequent analysis of these records may indicate courses of action which may effectively reduce the incidence of accidents.

Williams, who with Miles and other colleagues has carried out extensive research on wound infection in recent years, discusses the prevention of sepsis in industrial wounds. Few will disagree with the measures he advocates. Nevertheless it remains a fact that over the greater part of industry there are insufficient medical and nursing services to put them into practice. One day things may be different, but that day is still far off. It is perhaps worth considering whether or not there is a case for research designed to establish a good and effective treatment for industrial wounds which can be applied by the comparatively simple means available to the first-aid worker, who must still play an important role in the treatment of most minor industrial wounds.

John Rogan

* * *

Notes on Contributors

DR J. M. BARNES has been Director of the Medical Research Council's Toxicology Research Unit since its inception in 1947. The work of the Unit is devoted to a study of the mode of action of toxic substances which are of importance in industry and agriculture. During the past two years a major part of this work has been devoted to the examination of the toxic properties of the newer insecticides towards mammals. Dr Barnes' previous work has been mainly in the field of experimental pathology, and he has published papers on lymphocytes, lymph flow, arterial spasm, experimental pulmonary infections, anthrax, etc.

DR ETHEL BROWNING, formerly Assistant Pathologist to St Paul's Hospital, London, has been one of H.M. Medical Inspectors of Factories since 1940. In this capacity her special duties have included haematological and clinical examinations of industrial workers exposed to toxic agents, such as *x* rays, lead, and toxic solvents with dyshaemopoietic action—a field in which Dr Browning is an authority. She is author of *Toxicity of industrial organic solvents* (Industrial Health Research Board Report No. 80, 1937), a 2nd edition of which will be published shortly at the direction of the Toxicology Committee of the Medical Research Council. Dr Browning has also contributed various articles to medical literature, including, among many others, " Benzene as a toxic hazard in industry " and " Blood changes in luminizers using radioactive material ".

DR J. P. BULL is Assistant Director of the Medical Research Council's Industrial Medicine and Burns Research Units at the Birmingham Accident Hospital. After a period of research work on casualties caused by bombing, he served in the Royal Army Medical Corps from 1942 to 1946. He has recently been working on various problems encountered in the treatment of burns and industrial injuries. In collaboration with other authors, Dr Bull has written papers on such subjects as experiments with occlusive dressings of a new plastic, the impairment of sensation in burns and its clinical application as a test of the depth of skin loss, and a study of mortality in a burns research unit.

DR C. N. D. CRUICKSHANK is a member of the staff of the Medical Research Council's Industrial Medical Research Unit at the Birmingham Accident Hospital, and is engaged principally in clinical and environmental studies of industrial skin disease. He has also contributed to the study of industrial skin cancer, and of skin sensitization to chemicals. A number of Dr Cruickshank's publications on these subjects have appeared in the *British Journal of Industrial Medicine.*

DR E. F. EDSON was educated at the University of Sheffield. He served in the Royal Army Medical Corps from 1940 to 1947, being predominantly engaged upon toxicological and protective aspects concerning chemical warfare agents, in both temperate and hot climates. Since 1947 his appointment has been with the Division of Atomic Energy (Production) and he is a principal medical officer of the Ministry of Supply.

DR C. M. FLETCHER has been Director of the Pneumoconiosis Research Unit of the Medical Research Council since 1945.

During this period he has been concerned with investigations into all aspects of pneumoconiosis, particularly with the question of radiological diagnosis. Previously he had worked in the Department of Medicine, Postgraduate Medical School of London, at St Bartholomew's Hospital, and in the Nuffield Department of Medicine at Oxford, where he carried out the first trials on penicillin (*Lancet*, 1941, **2**, 177).

DR J. GOUGH is Professor of Pathology and Bacteriology at the Welsh National School of Medicine, Adviser in Pathology to the Welsh Regional Hospital Board and Honorary Consultant Pathologist to the United Cardiff Hospitals. Professor Gough has for many years carried out research on pneumoconiosis, devoting his attention particularly to the pulmonary disease found in coalworkers. He showed that lung changes in coalminers were identical with those in coaltrimmers (men loading coal into ships) and that they were due to the same cause, the breathing of high concentrations of coal dust—which until ten years ago had been held to be harmless. He also pointed out the occurrence of a characteristic focal emphysema. With Dr J. E. Wentworth, he developed a technique of cutting and mounting thin sections of entire organs for comparison with radiographs. Professor Gough is the author of many articles on pneumoconiosis.

DR DONALD HUNTER received his medical education at the London Hospital, where he has been Physician since 1927. In 1929 he was elected Fellow of the Royal College of Physicians. Since 1925, when he was appointed Research Fellow in Industrial Medicine at the Harvard Medical School, Boston, USA, Dr Hunter has been acknowledged as an authority on industrial diseases, particularly those arising from contact with lead. Dr Hunter was invited to give the Croonian Lectures of the Royal College of Physicians for 1942; these took the form of a review of the effects of toxic substances encountered in industry, dealing mainly with the metals, aromatic compounds, chlorinated hydrocarbons and the glycol group. He was appointed Director of the Medical Research Council's Department for Research in Industrial Medicine at the London Hospital at its inception in 1943. In the present year, 1950, Dr Hunter is visiting Australia in the capacity of William McIlrath Guest Professor of Medicine to the Royal Prince Alfred Hospital, Sydney. He has contributed many papers to scientific and medical journals, and has been editor of the *British Journal of Industrial Medicine* since publication of the journal began in 1944. He is the author of two textbooks: *Clinical methods* (with Sir Robert Hutchison), 12th ed., 1949, and *Occupational diseases*, 1935.

DR J. F. LOUTIT was formerly Medical Officer in charge of the South London Blood Supply Depot, Sutton, and previously held a number of hospital appointments. In 1947 the Medical Research Council's Radiobiological Research Unit was established under his directorship at the Atomic Energy Research Establishment, Harwell, Berkshire. Dr Loutit has contributed a number of articles to various scientific journals.

DR E. L. MIDDLETON was educated at Edinburgh where he graduated in 1909. From 1911 to 1921 he was engaged in the tuberculosis service and, during this period, he made a clinical study of silicosis among workers exposed to the dust of millstone grit in North Wales. For 26 years from 1921 he was Medical Inspector of Factories at the Home Office where he carried out many clinical and environmental investigations into the hazards of dust in various occupations, and contributed official reports and articles to the medical literature on that subject. Dr Middleton was Secretary of the Medical Research Council's Committee on Industrial Pulmonary Disease at its formation in 1930. As British Government delegate he attended the international conferences on pneumoconiosis, held under the auspices of the International Labour Office (ILO), at Johannesburg in 1930, at Geneva in 1938, and at Sydney in 1950. He was Milroy lecturer at the Royal College of Physicians, London, in 1936, and is a member of the ILO Correspondence Committee and of the Permanent International Committee on Industrial Medicine.

DR R. S. F. SCHILLING is Reader in the Department of Occupational Health at Manchester University. He was at one time one of H.M. Medical Inspectors of Factories, and Secretary of the Industrial Health Research Board of the Medical Research Council. He has undertaken various studies on industrial health problems, including clinical and environmental investigations of the handling of inorganic compounds of arsenic, fluoride intoxication in magnesium factories, and the exposure of paint mixers to organic solvents. Present work has included extensive field investigations among textile workers.

PROFESSOR JOHN R. SQUIRE has been Leith Professor of Experimental Pathology and Director of the Department of Pathological Studies at the University of Birmingham since 1948. He is also Honorary Director of the Medical Research Council's Industrial Medicine Research Unit and Burns Research Unit at the Birmingham Accident Hospital. During the last war he was on the staff of the Scientific Adviser to the Army Council. He was later with the Operational Research Section in Burma, and, afterwards, O.C. Biological Research Team in South-East Asia. Professor Squire's scientific work has included studies on blood clotting and shock (1936–40), on asthma due to horse dandruff (1940–42), and on biological problems of warfare (1942–46). His most recent work has been in the field of industrial medicine, with particular reference to the control of infection in small wounds, industrial skin disease, industrial skin cancer, and the treatment of burns.

DR H. TAYLOR was educated at the Universities of Manchester and Cambridge, gaining his M.Sc. at the former, and his Ph.D. at the latter. From 1926 to 1930 he was engaged in physiological research for the Chemical Defence Department of the Ministry of Supply, and from 1930 to 1934 was on the staff of Edinburgh University in the Departments of Animal Genetics and Medical Chemistry. Since 1934, when he joined the staff of Imperial Chemical Industries Ltd., Dr Taylor has been engaged in research work on problems of industrial hygiene, with particular reference to the toxicology of industrial products.

DR ELIZABETH TOPLEY is working on the staff of the Medical Research Council's Industrial Medicine and Burns Research Units at the Birmingham Accident Hospital. She is principally engaged on the application of bacteriology to the clinical problems of dermatitis and burns. In collaboration with Dr S. H. Harrison, Dr Topley contributed a paper on the value of systemic penicillin in finger pulp infection to the Ninth International Congress on Industrial Medicine, which was held in London in 1948. Other articles have been published in the *Lancet* and in *Clinical Science*.

MR J. W. WHITFIELD is a member of the Medical Research Council's scientific staff at the Psychological Laboratory, Cambridge. He was a scholar of St. John's College, Cambridge, whence he graduated in 1939. He is a member of the British Psychological Society, a foundation member of the Experimental Psychology Group and a member of the editorial board of the *Quarterly Journal of Experimental Psychology*. In the field of applied psychology he has worked on accident causation and on the relation between sickness and industrial fatigue. Mr Whitfield has also worked on the problems of statistical design suitable for psychological data, and, in recent years, has been particularly concerned with the developments in ranking statistics.

DR R. E. O. WILLIAMS graduated from University College, London, and University College Hospital. From 1942 to 1946 he worked in the Medical Research Council's Wound Infection Research Unit at the Birmingham Accident Hospital where he carried out extensive investigations into the cause and prevention of infection and sepsis in small industrial wounds, and into cross-infection in hospital wards. Concurrently he carried out a number of studies on the prevalence of staphylococcal carriers among healthy adults, and on the bacteriology of staphylococci. In 1946 he joined the Public Health Laboratory Service and worked on air-borne infection; he is now Director of the Streptococcal and Staphylococcal Reference Laboratory at Colindale, London.

TOXICOLOGY OF SOME METALS AND THEIR COMPOUNDS USED IN INDUSTRY

DONALD HUNTER M.D. F.R.C.P.

Director, Department for Research in Industrial Medicine
Medical Research Council
London Hospital

1 Beryllium
  a Symptoms and signs of exposure
  b Radiographic changes, and pathology
  c Diagnosis
  d Prevention
2 Cadmium
3 Chromium
  a Symptoms and signs of exposure
  b Prevention
4 Manganese
5 Osmium
6 Platinum
7 Selenium
  a Selenium in soils
  b Selenium in industry
  c Prevention
8 Tellurium
9 Uranium
10 Vanadium
References

A metal may enter the tissues without acting as a poison. Thus silver produces no toxic symptoms although it can bring about lifelong disfigurement in the form of generalized argyria. Other metals, which are themselves harmless, nevertheless form certain toxic compounds. For example, both nickel and tin are innocent of toxic effects, yet nickel carbonyl and tin tetrahydride are intensely poisonous.

A metal or a compound of a metal may have a different effect according to whether it exists in organic or inorganic form, whether its physical properties are those of a solid, liquid or gas, whether the valency of the metal radical is high or low, or whether it falls upon the skin or enters through the respiratory or alimentary tract. Thus, men poisoned by tetraethyl lead show cerebral symptoms and signs, the well-known symptoms of poisoning by inorganic compounds of lead being absent. Arsine acts as a powerful haemolytic poison, whereas the inorganic compounds of arsenic never produce this effect. The physical form in which a metallic compound exists in the atmosphere may determine its toxicity; zinc oxide, for example, produces fever and rigors when inhaled as freshly formed fume, and yet it is inert when inhaled as dust. The effects of a metallic poison may differ according to its portal of entry; for instance, workers exposed to the vapour of mercury may suffer from tremor, whereas this symptom does not occur when mercury is rubbed into the skin.

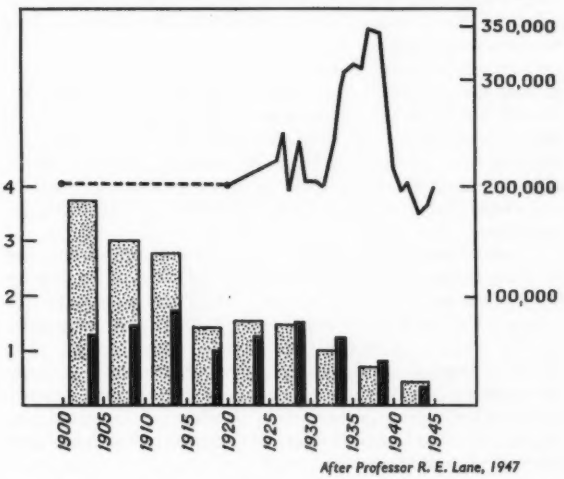
Knowledge gained during many years has made it possible for physicians, working in collaboration with chemists, physicists, and engineers, to control the occupational hazards encountered in handling such substances as lead, mercury and arsenic and their compounds. Thus, despite a steady increase in the consumption of lead in the United Kingdom, the incidence of lead poisoning in Great Britain has fallen steadily throughout the present century (fig. 1). From time to time these old offenders are used in new ways and they may then give rise to unexpected cases of poisoning.

In the development of new alloys many metals, rare or unknown a few years ago, are now assuming commercial importance. So far no toxic effect has been discovered in workers handling cerium, gallium, indium, molybdenum, rhenium, titanium, tungsten or zirconium. On the other hand, toxic effects from beryllium, cadmium, osmium, platinum, selenium, tellurium, uranium and vanadium have already been observed. This review concerns mainly the toxicity of the latter group of metals, the use of which has been newly developed in industry. The effects of lead, mercury and arsenic are not discussed, but chromium and manganese are included because of a great increase in their use in recent years.

1. Beryllium

Beryllium is a very light metal, having about the same density as magnesium. It is hard and shiny and resembles steel in appearance and lustre. It occurs in nature as beryllium aluminium silicate or beryl, $3BeO.Al_2O_3.6SiO_2$. It was

FIG. 1. NOTIFIED CASES OF LEAD POISONING 1900–45 SHOWN IN FIVE-YEAR PERIODS



After Professor R. E. Lane, 1947

Figure shows the steady fall in the incidence of lead poisoning in Great Britain in spite of a persistent rise in the consumption of lead in the United Kingdom

Broken and continuous line on the graph shows consumption of lead in the United Kingdom. (No figures are available for the period before 1920.)

Left-hand ordinates show:
total number of cases of lead poisoning in thousands
total number of deaths from lead poisoning in hundreds

Right-hand ordinates show:
consumption of lead in tons

FIG. 2. REMOVAL OF BERYLLIUM DUST

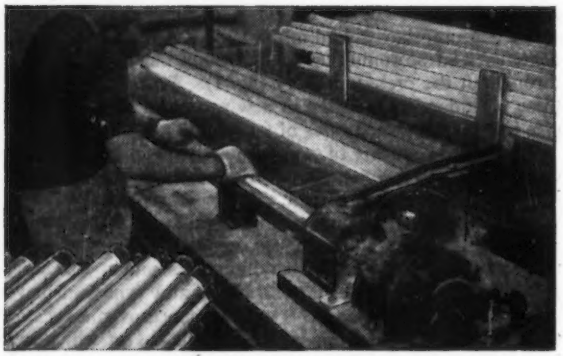


Figure shows the removal of dust produced in brushing clean the ends of the fluorescent lamp tubes by exhaust ventilation locally applied

the appreciation of the properties of the alloys of beryllium which first increased its value. The principal alloy is beryllium-copper which is hard, resistant to corrosion, non-rusting, non-sparking and non-magnetic. It has a tensile strength as great as mild steel and six times that of copper. Metallic beryllium is employed as a deoxidizer in steel making. In the atomic energy industry pure beryllium rods are essential to the efficient working of the graphite pile. Industrial radiography has created a demand for pure beryllium foil for the windows of *x*-ray tubes; the metal allows the passage of long wavelength radiation.

Occupations involving exposure to beryllium compounds include the extraction of the metal from the ore, the preparation of beryllium steel, the manufacture and cutting of beryllium-copper alloys, and the making of beryllium-containing crystals for radio apparatus. In addition, there may be exposure to beryllium oxide used as a refractory for making crucibles, and to beryl in the manufacture of electrical porcelain.

A considerable hazard exists in preparing and mixing the powders used as phosphors for coating the tubes of fluorescent strip lamps and certain tubes used for electric signs. In this industry the compounds used are zinc beryllium manganese silicate, zinc beryllium silicate and beryllium oxide. The tubing is coated on the inside by pumping into it a liquid suspension of the phosphor, excess of which is then drained away. Dry mixing of the powder, spillage of the liquid suspension and the brushing clean of the ends of the tubes may produce considerable amounts of dust (fig. 2).

a. Symptoms and Signs of Exposure

Symptoms attributable to exposure to beryllium compounds include conjunctivitis, irritation of the upper respiratory tract, dermatitis, subcutaneous granulomata, and acute and chronic forms of lung disease (Machle, Beyer & Tebrock, 1949). Conjunctivitis is frequently associated with dermatitis of the face. It follows exposure to soluble salts of beryllium in industrial plants where the ore is processed or where the halides and acid salts are handled. On removal from contact the lesions readily heal. Exposure to the soluble salts may also cause irritation of the nose and throat, with epistaxis, and swelling and redness of the mucous membranes. Tracheobronchitis may develop, together with anorexia and dyspnoea, and there may be loss of weight. The symptoms and signs clear up completely within two or three weeks after exposure ceases, and no special treatment is required.

Dermatitis may be severe and may lead to sensitization. The lesion is usually an oedematous papulovesicular eruption appearing mainly on the exposed surfaces. Healing occurs promptly on removal from contact and is hastened by local treatment of the lesion. Subcutaneous granulomata occur when beryllium compounds are introduced beneath the skin (Grier, Nash & Freiman, 1948). Such lesions may occur in persons who have cut themselves on broken fluorescent lamps. The granuloma may measure as much as 2.5 by 2.0 cm. in diameter (Plate II, fig. B). It is necessary to excise the granulomatous mass and to remove completely all beryllium from the lesion or healing may be delayed.

The pulmonary lesions are much more serious and disabling. The first cases of the acute disease were reported from the USA in 1943 by Van Ordstrand, Hughes & Carmody. In 1946, Hardy & Tabershaw described cases of a chronic lung disease occurring among employees of a firm manufacturing fluorescent lamps in Salem, Massachusetts. It was the resemblance between these chronic cases and sarcoidosis which led to the designation Salem sarcoid. In 1949 Aub & Grier reported seven cases of acute pneumonitis in metallurgical workers exposed to the dust and fume of pure beryllium metal and beryllium oxide. The occurrence of such cases supports the view that the beryllium ion is toxic in its own right and that the poisonous effects of soluble beryllium salts are not to be attributed to the acid radicals. In 1949 Machle *et al.* reported more than 400 cases of lung disease which had occurred in beryllium workers in the USA. One hundred and twenty-three of these patients showed the delayed pneumonitis known also as chronic berylliosis or pulmonary granulomatosis of beryllium workers.

The symptoms of the acute disease are those of a chemical pneumonitis. They occur during employment. In the early stages cough with blood-stained sputum is accompanied by retrosternal pain, dyspnoea, cyanosis and loss of weight. Non-productive cough may be present for several days before dyspnoea on exertion ; later, dyspnoea at rest becomes obvious. Rapid respiration, anorexia and marked prostration follow. Usually there is no fever, but cyanosis and tachycardia are present and râles are heard over both lungs. Death may occur within two weeks. The morbid anatomy of the lungs is similar to that of acute chemical pneumonitis from other causes except that there is less evidence of necrosis. The alveoli are filled with exudate composed of oedematous fluid and fibrin containing macrophages. Collections of lymphocytes and plasma cells occur in the septa. In cases where death has occurred after several weeks there are large areas of fibroblastic proliferation such as are seen in organizing pneumonia. More commonly, resolution begins in the third week of the illness and is complete in from five weeks to five months. Serious sequelae are unusual, but attacks of the acute illness have been followed by the onset of chronic berylliosis after two years (Machle *et al.* 1949). Symptoms and signs precede radiological changes in the lungs by several weeks. On the *x*-ray plate linear markings and a granular ground-glass appearance suggesting pulmonary congestion appear first. The shadows are diffuse but may be less marked at the apices and bases owing to compensatory emphysema.

Consolidation may follow. As the clinical signs disappear the lung lesion becomes granular and nodular with conglomerate masses. In from one to four months these disappear leaving residual fibrosis in some cases.

The first symptoms of the chronic disease are variable and may not appear for as long as six years after the last exposure to beryllium compounds. The majority of cases have occurred in employees in the fluorescent lamp industry, but two laboratory workers and at least ten people living in the neighbourhood of factories using beryllium compounds have been affected. Less than 5% of the persons exposed have developed the disease. This suggests that some people are unduly susceptible to the effects of absorption of small amounts of beryllium. The United States Atomic Energy Commission has investigated the contamination of the atmosphere in the neighbourhood of a plant producing beryllium oxide, beryllium-copper and beryllium metal. During the preceding ten years 1,600 workers had been employed. In contrast to five known cases of the chronic disease within the factory, ten cases, of which at least one was fatal, occurred in persons living within three-quarters of a mile of the plant, though they had never worked there. The atmospheric concentration of beryllium three-quarters of a mile away from the factory ranged from 0.01 to 0.1 μg. per cubic metre (Eisenbud *et al.* 1949).

Vague ill-health, slight but persistent loss of weight, weakness and lack of energy, or an unusually persistent upper respiratory tract infection may herald the onset of the disease. It may be weeks or months before abnormal signs appear in the lungs. Weakness, anorexia, and progressive loss of weight which may be as much as 20 to 30 lb. (9.07 to 13.61 kg.) in a month become prominent symptoms and persist throughout the illness. Cough with little sputum, worse in the mornings or on exertion, is constantly present and bears no relationship to the severity of the disease or to the radiographic signs. Dyspnoea is extreme and may be the presenting symptom. Tachycardia, particularly when there is cyanosis, is associated with a normal or low blood-pressure. Clubbing of the fingers develops in the later stages. Cardiac failure occurs, increasing the dyspnoea and later causing orthopnoea and oedema of the extremities. Approximately one-third of the patients die, and one-third are permanently disabled and remain in great pulmonary distress. The rest lose their symptoms, the lung changes resolving to some extent.

b. Radiographic Changes, and Pathology

The earliest change in the radiograph is a diffuse finely granular appearance homogeneously distributed throughout both lungs. The apices and bases are involved. Paratracheal masses and enlarged hilar shadows are seen in many cases. As the disease progresses fine nodulation appears on a granular background (Plate I, fig. A). Confluence of nodules may occur, but it is much less evident than in silicosis. Later there is lobular emphysema, particularly at the apices and bases. Signs of cor pulmonale may develop, and spontaneous pneumothorax, without pleural effusion, has occurred in a few cases. The *x*-ray appearances alone are not diagnostic.

The pathological findings in chronic berylliosis resemble closely those found in sarcoidosis. The lungs are grossly emphysematous, with scattered fine nodules and diffuse interstitial fibrosis. Granulomata are formed within the alveolar spaces by organization of exudate. They have a fibrinoid centre with peripheral fibrosis and varying degrees of mononuclear infiltration, together with numerous giant cells of the Langhans type. Similar lesions have been found in the skin and subcutaneous tissues, in hilar and axillary lymph nodes, and in the liver. Mid-zonal necrosis is also found in the liver.

c. Diagnosis

Diagnosis depends upon an occupational history of significant exposure to beryllium compounds, a characteristic onset and course of the disease, *x*-ray findings, and the presence of beryllium in the urine and tissues. Differentiation from sarcoidosis, chronic miliary tuberculosis, fungus infections, primary pulmonary fibrosis, diffuse nodular silicosis, miliary carcinomatosis, mitral stenosis, and siderosis may be difficult. A diagnosis of chronic berylliosis can only be made by considering the whole picture, together with evidence of significant exposure to beryllium compounds. Treatment is symptomatic. In patients severely affected, oxygen relieves the dyspnoea. Penicillin-streptomycin aerosol therapy has relieved secondary bacterial infection but has no other beneficial effect. Attempts to increase the rate of elimination of beryllium with injections of 2 : 3-dimercaptopropanol (BAL) have not been successful, nor has any other therapeutic measure influenced the course of the disease.

d. Prevention

In Great Britain in 1949 poisoning by beryllium and its compounds was added to the list of diseases prescribed under the National Insurance (Industrial Injuries) Act, 1946. In the manufacture of fluorescent lamps, halophosphates, which contain no beryllium, must be used in place of the poisonous phosphors formerly used. Preventive measures must be enforced in all industries where beryllium and its compounds are handled. Every effort must be made by engineering methods to keep the atmospheric concentration at the lowest possible level. Protective clothing and adequate laundry services should be provided.

Workers at risk should be seen at regular intervals by a doctor and questioned about suggestive symptoms. They should be weighed at monthly intervals, and have their chests *x*-rayed at least once a year. Repeated medical and *x*-ray examinations must be made of all workers who have unexplained symptoms, particularly when these suggest disease of the respiratory system. Since subcutaneous granulomata have developed in persons who have cut themselves on broken lamps, caution must be exercised in the disposal and salvage of burnt-out fluorescent lamp tubes. The existence of the hazard of non-occupational beryllium poisoning in the neighbourhood of factories handling this substance presents a challenge not only to those responsible for industrial health but also to public health authorities in industrial communities in general. Indirectly, therefore, the splitting of the atom has given us new and grave responsibilities besides those connected with radioactive substances.

2. Cadmium

Cadmium (Cd) is extracted from zinc ores in the course of smelting. It is used in the manufacture of alloys and in making ceramics and cadmium vapour lamps. The rust-proofing of iron and steel articles by the method of cadmium electroplating has to some extent replaced that of coating

with zinc. The principal industrial hazards arise in the smelting of ores, the welding of alloys, and the firing or welding of cadmium-plated metal.

In 1923 Legge reported three cases of cadmium poisoning, one of them fatal, in men in a paint factory where ingots of cadmium had been melted during a period of three hours in a poorly ventilated room. All three men complained of dryness of the throat, headache and nausea. The urine was coloured brown. A necropsy on the man who died showed hyperaemia of the bronchi, gastrointestinal tract and kidneys (Legge, 1924). In 1942 Nasatir reported a fatal case. Death occurred on the fifth day after exposure to cadmium fume caused by burning off, with an oxy-acetylene flame, deposits of metal containing a high percentage of cadmium. The symptoms were a feeling of constriction of the chest, increasing dyspnoea, and cough which became much worse before death.

In 1944 Spolyar, Keppler & Porter wrote an extensive report on five cases of cadmium poisoning, one of which died, resulting from exposure to cadmium oxide during flanging operations on cadmium-plated pipe. On the basis of the 59 cases reported up to that date the mortality rate of industrial cadmium poisoning appears to be 15 %. In 1941 Johnstone reported the case of a young Mexican labourer who was sent to hospital after he had used an oxy-acetylene torch on the inside walls of a furnace in which cadmium residues had been recovered from scrap metal. The patient was extremely ill with severe dyspnoea and exhaustion and he gave a history of headache, cough and pain in the chest. The temperature rose to 104° F. (40° C.), with a pulse rate of 140, and a respiratory rate of 50, per minute. Patchy signs appeared in the chest and bronchopneumonia was revealed by *x* rays. Cyanosis and increasing respiratory distress preceded death. At necropsy the lungs showed confluent bronchopneumonia.

In 1944 Ross described mass poisoning due to cadmium oxide fume affecting 23 workers. Finely divided cadmium dust from a cadmium recovery chamber became ignited owing to red-hot cigarette ash carelessly dropped by one of the workers. In a few minutes the cadmium dust became incandescent and emitted clouds of cadmium oxide fume. The victims complained of irritation of the eyes, headache, vertigo, dryness of the throat, cough, constriction of the chest and weakness of the legs. Three hours later delayed effects were observed; these included shivering, sweating, nausea, epigastric pain and dyspnoea. No case was fatal.

When cadmium-coated metal is heated, dangerous quantities of cadmium oxide are formed and volatilized. It has therefore been suggested that cadmium-coated metal should be labelled. While this measure is effective for large pieces it is somewhat difficult to ensure that small objects so coated are labelled (Fairhall, 1946).

3. Chromium

Chromium is a silver-white, hard, brittle metal. It is derived from one ore only, chromite or chrome ironstone, $FeO.Cr_2O_3$. Approximately 45 % of the world's supply is used for alloys, about 40 % for refractories, and 15 % for chemical purposes. Chromium is an essential component of the hard, high-strength steels used in engineering, and also of stainless and rustless steels. Alloys resistant to corrosion, such as stainless chromium-nickel steel, are extensively used in the chemical industry. The alloy steels are manufactured directly from ferro-chrome, a chromium-iron alloy prepared by reducing chromite in an electric furnace in the presence of carbon. For refractory purposes the crude ore is embodied in bricks, cements and plasters used in the construction of furnaces. The only commercial use of pure chromium metal is in the form of electroplate. Chrome chemicals are used in the plating and anodising of metals, in the tanning of leather and in the manufacture of pigments.

Chromium compounds used in the chemical industry are obtained from the basic chromates, sodium and potassium dichromate or monochromate. These compounds are prepared from chromite which is crushed, mixed with dolomite and the carbonate of sodium or potassium, and heated in a rotary furnace for eight hours at a temperature of 1,200° C. In many factories the rotary furnace has replaced the reverberatory furnace only since 1938. The oxide is converted to monochromate and the frit from the furnace is carried to washing or leaching tanks arranged in series. The monochromate is dissolved out by repeated washings with water and the concentrated liquor containing monochromate is treated with sulphuric acid. Dichromate is formed by double decomposition, and sodium sulphate is a by-product of the process. In some factories in Germany and the USA the residue from the leaching tanks is dried, crushed and used over again in the process. This residue contains up to 1 % of monochromate. In Great Britain no attempt is made to extract this small remaining quantity of chromate; the residue is removed from the leaching tanks in a moist state and discarded.

The toxicity of chromium compounds is determined by the valency of the metal radical. The toxic action is confined to the compounds of hexavalent chromium. Trivalent chromium salts such as the phosphate and carbonate are harmless (Akatsuka & Fairhall, 1934). Air contaminated with chromic acid mist or with the dust from chromates or bichromates is the principal source of exposure in industry. The process of chromium plating consists in wiring the articles to a frame ready for the plating vat, the initial plating which lasts up to 15 minutes, and the unwiring, swilling and polishing of the plated articles. The solution in the plating tank contains 50 % of chromic acid, and during electrolysis reddish-brown fumes which contain 60 % of chromic acid are forced up in the form of a mist by the evolution of hydrogen at the cathode. In anodising, a coating highly resistant to corrosion is formed on aluminium and its alloys through the anodic oxidation of the aluminium. Chromic acid is used as the solution in which the anodising operations are carried out (fig. 3), and the hydrogen liberated at the cathode carries a significant amount of chromic acid mist into the atmosphere along with it (Zvaifler, 1944).

a. Symptoms and Signs of Exposure

Lesions of the skin due to chromium salts have been known since 1826, when "chrome holes" on the fingers and hands of bichromate workers in Glasgow were described as ". . . troublesome sores . . . which gradually pierced deeper and deeper" (see *Edinburgh Medical and Surgical Journal*, 1826). The chromates and bichromates of potassium and sodium, and chromic acid, may cause either dermatitis or localized ulceration according to whether trauma is present or not. Exposure to these substances occurs in chromium platers, colour workers and french polishers. Dermatitis may occur on the hands, arms, face and chest. The onset is sudden,

FIG. 3. CHROMIUM PLATING

After R. T. Johnstone, 1948

a: Chromic acid mist produced during the anodic oxidation of aluminium

b: Removal of chromic acid mist by exhaust ventilation locally applied

but it is unusual for an attack to occur until the operator has been at the work for at least six months. In severe cases the face is intensely red and swollen, and the affected parts itch a great deal and may become painful (Trumper, 1931). Fair-haired people are particularly prone to a chrome dermatitis and their employment calls for peculiar care (Horner, 1934).

Chrome ulcers begin in abrasions of the skin and are most commonly found at the root of the finger-nail, the knuckle of the hand or the dorsum of the foot. They are circular in shape, clear-cut, usually 1 cm. or less in diameter, and look as if punched out, hence the name " chrome hole " (Plate II, fig. C). They have a strong tendency to heal but may penetrate very deeply, even to the bone. Although painless they itch intolerably at night. If neglected, an ulcer may lead to infection of the adjacent joint causing loss of the finger. There is no tendency towards malignant change. The dust of chromium salts and the mist of chromic acid may produce ulcers on the eyelids or the edge of the nostrils.

The mucous membrane of the nose is commonly affected; if so, perforation of the nasal septum occurs. Usually this causes no inconvenience and is discovered accidentally. Legge (1902) examined 176 men employed in the manufacture of potassium bichromate. In 126 the septum was perforated, and in 20 it was ulcerated. In none of the 30 men in whom the septum was found to be normal was the immunity attributable to shortness of exposure, indeed one-half of them had been employed for upwards of 10 years. The process begins with sneezing and the symptoms of nasal catarrh. The pain accompanying the ulceration seems to be insignificant. It is never severe enough to necessitate absence from work or to need treatment. Once the perforation is established, the only inconvenience is the formation of plugs of mucus in the nasal passages. The general health is unaffected by the condition. In 1922 Legge pointed out that although constant irritation of the skin and mucous membranes by chromium compounds resulted in chronic ulceration and the active destruction of tissues, epitheliomatous change did not occur in these lesions. In 175 cases of chrome ulceration recorded in the British industry at this time no single case showed any sign of epithelioma. Greenburg *et al.* (1942) carried out a survey of 106 painters in an aeroplane factory, and found five cases of perforation of the nasal septum in men employed on spray-painting with a paint containing zinc chromate.

A high incidence of cancer of the lung in the chromate-producing industry has been reported from Germany and the USA. The evidence upon which such reports are based is inconclusive and the question must be regarded as unsettled.

b. Prevention

The preventive measures necessary in handling chromic acid, chromates and bichromates include the removal of dust and mist, cleanliness, regular medical supervision, and the covering up of cuts and abrasions with suitable dressings. The prevention of danger in chromium plating and anodising

depends on the correct design of the vats to include exhaust ventilation. It may often be necessary to provide rubber gloves, boots, and apron for a person working round the chromic acid tanks, but, unless well-designed, these are not always of great value. The workers have to reach up to lift out the metal parts and hang them on hooks, and if the gloves are loose at the wrists the solution that drips on to the arms may, when the hands are lowered, run down inside the gloves. The solution may also run down inside the boots if they are loose at the top (Hamilton & Hardy, 1949). The exposed skin should be washed and carefully dried. Application of an ointment made up of equal parts of lanolin and soft paraffin is useful. Soft paraffin should be freely applied through the anterior nares to the nasal septum. Weekly inspection of the nasal passages should be regularly carried out for all workers by the nurse, and less frequent inspection should be made by the works' doctor.

4. Manganese

The most important ore of manganese is the black dioxide, MnO_2, known as pyrolusite. About 95% of the world production of manganese is used for metallurgical purposes, particularly the manufacture of manganese alloy steel. During the process of steel making, ferro-manganese is added to the furnace charge to prevent the formation of iron oxide and sulphide in the finished steel. In the chemical industry manganese dioxide is the starting-point in the manufacture of all manganese preparations. It is used for dry batteries and in the pottery, soap, and colour industries. Manganates and permanganates are used for preserving wood, for bleaching textiles, and for disinfecting and oxidizing purposes.

In 1837 Couper described two severe cases of poisoning in men employed in grinding manganese dioxide in the manufacture of bleaching powder. These men had spastic weakness of the lower limbs, with an unsteady gait. The arms were less affected, and there was no tremor (Couper, 1837a, 1837b). In 1919, Edsall, Wilbur & Drinker published an article on manganese poisoning resulting from inhalation of manganese dust in a separating mill. The first cases recognized in Great Britain were reported by Charles in 1922. The men had been exposed to the dusts of manganese ores for periods ranging from nine months to three years and had been incapacitated for work for three to five years. The symptoms and signs indicate involvement of the extrapyramidal motor system. They include languor and sleepiness, low monotonous voice, mask-like facies, involuntary movements varying in degree from a fine tremor of the hands to gross rhythmical movements of the arms, legs, trunk, and head, cramps in the calves, retropulsion and propulsion, unsteady gait, and occasionally uncontrollable laughter or weeping. There is no disability except in the nervous system and although men seriously poisoned are lifelong cripples, the condition is not lethal.

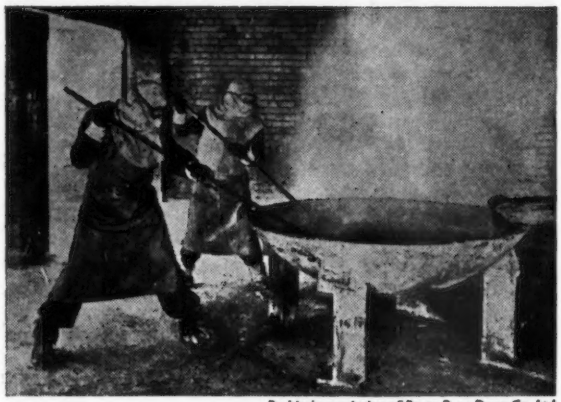
Cases have been caused by the inhalation of excessive amounts of dust in the mining, grinding, sorting, sieving, packing and loading of manganese ores and in the manufacture of manganese steel. In Great Britain no case has been recognized in workers manufacturing dry batteries.

In 1921 Brezina first drew attention to the unusually high incidence of pneumonia in men handling manganese ores. He reported that five out of ten men working in a pyrolusite mill had died of pneumonia in two years. In 1933 Baader ascribed the high incidence of pneumonia amongst dry-battery workers to manganese dioxide, while Heine (1943) pointed out the high incidence of pneumonia in men handling pyrolusite in German factories. The erection, in 1923, of an electrical plant for manganese smelting at Sauda in Norway was followed by a tenfold increase in the mortality rate for pneumonia in that area. A pall of smoke which overhung the town was found to contain particles of oxides of manganese, less than 5 μ in size (Riddervold & Halvorsen, 1943).

Lloyd Davies (1946) described his observations on men employed in the manufacture of potassium permanganate. The manganese content of the atmospheric dust to which they were exposed, expressed as manganese dioxide, varied from 41 to 66%; practically all the particles were below 1 μ in size, and 80% were less than 0.2 μ. Besides a high incidence of pharyngitis and bronchitis they showed an incidence of pneumonia which varied from 1,500 to 6,300 per 100,000 in the period 1938 to 1945, compared with an average of 73 for the same period among the rest of the male employees. The response to sulphonamides and resolution of the lung were slower than in ordinary lobar pneumonia but no persisting pulmonary lesions were observed either clinically or radiographically.

Manganese poisoning can be prevented by the application of local exhaust ventilation, both at the furnace to remove fume and at the packing and sieving apparatus to remove dust. Respirators may be worn which combine active charcoal to absorb the vapours and a cotton wool filter to trap the dust. Personal hygiene is important and the worker must wear protective clothing and gloves (fig. 4), because the occurrence of absorption through the skin has been established. These measures give good results. Applied in one particular factory they removed all risk of poisoning over a period of six years.

FIG. 4. PREVENTION OF MANGANESE POISONING: USE OF RESPIRATORS AND PROTECTIVE CLOTHING



By kind permission of Boots Pure Drug Co. Ltd.

Workers stirring manganese dioxide, melted caustic potash, and lime, in the manufacture of potassium permanganate. In the violent reaction which ensues, volumes of steam and quantities of dust are emitted

5. Osmium

Osmium (Os) occurs among the platinum group of metals as the alloy osmiridium. It is one of the denser known substances, being about three times as heavy as iron. Osmiridium is exceptionally hard and is therefore used for the tips of the gold nibs of fountain pens. It is also used for electrical contacts, as a catalyst in the preparation of synthetic ammonia, and for measuring the rapidity of explosion of guncotton. Osmium itself is innocuous but the volatile osmium tetroxide, commonly called osmic acid, is slowly formed on exposure of the spongy metal to air. Osmium tetroxide has a very irritating odour, resembling bromine, and attacks the nose and eyes. The vapour has a sudden vigorous effect on the mucosa of the nose, pharynx and bronchi, likened by workmen to the kick of a mule. If fairly high concentrations are inhaled there is a sense of momentary constriction of the chest and inability to breathe, the aftermath of which may persist for 12 hours. Deville & Debray (1859), the first chemists to make an extensive study of osmium compounds, described how the vapour of osmic acid attacked their eyes. One of them developed conjunctivitis which interfered with vision for some weeks.

Raymond (1874) reported a fatal case of poisoning which occurred in a Paris workman. The vapour of osmium tetroxide had caused capillary bronchitis followed by bronchopneumonia. Necropsy revealed purulent bronchitis and confluent bronchopneumonia. Brunot (1933) exposed himself to the vapour of osmic acid and found that a smarting sensation in the eyes was followed by lachrymation and the appearance of haloes around bright lights. He then exposed rabbits until they died of bronchopneumonia. Post-mortem examination showed dark red consolidation with scattered purple areas in the lungs. The bronchi were filled with pus, and the kidneys showed cloudy swelling. He also placed one drop of 1% osmium tetroxide in water into the conjunctival sacs of rabbits. After 24 hours there was oedema and swelling of the eyelids with profuse purulent discharge and a metallic brown stain on all parts of the conjunctiva. After 48 hours there were superficial ulcers in the conjunctiva and the cornea was milky and semi-opaque. Ten days after exposure the acute stage had subsided, but there was corneal opacity, and a pannus began to form which after one month slowly extended towards the centre of the cornea.

McLaughlin, Milton & Perry (1946) recorded the effects of osmium tetroxide in seven men engaged in refining osmiridium. The hazard arose from the fine mist or spray containing osmic acid which came off the reaction vessels when the ore containing the precious metals was dissolved in aqua regia. The men exposed had smarting of the eyes with lachrymation and sometimes frontal or orbital headache. They saw haloes round lights, one man saying they were green in the centre and red round the outside. When the symptoms were most severe they were unable to read or to see the images on a cinema screen. Their eyes were always normal by the next day. Only one man complained of cough and expectoration. No chronic or cumulative effects were noted. Histologists who use osmic acid as a stain for myelin and fat are familiar with the headache which comes on if the bottle is left unstoppered on the bench. Because of the blackening of osmium tetroxide in contact with oil and fat, an aqueous solution of osmic acid was at one time used for taking finger-prints. The method was given up because it was soon realized that it caused dermatitis.

Preventive treatment of osmic acid poisoning consists of the proper ventilation of reaction vessels and other apparatus giving off osmium tetroxide. It is clear that the vapour of this substance must not be allowed to enter the atmosphere of the workroom.

6. Platinum

Platinum (Pt) is a silver-white metal, tenacious, very malleable, ductile and softer than silver. It has many uses in the chemical and electrical industries. Exposure to platinum in industry occurs in the metallurgical and chemical processes used in the preparation of the metal and its salts.

Platinum was considered relatively harmless until 1945 when Hunter, Milton & Perry published the results of their investigation of four platinum refineries. They found that, of 91 workers exposed to the dust or spray of complex salts of platinum, 52 suffered from running of the nose, sneezing, tightness of the chest, shortness of breath, cyanosis, wheezing, and cough. Thirteen of the men complained of dermatitis. None of these symptoms was apparent in the workers exposed to metallic platinum dust only, or to the complex salts of the other precious metals, including palladium. The platinum content of the air samples taken at various stations throughout the works was determined spectrographically and found to vary from 5 μg. to 70 μg. per cubic metre (Fothergill, Withers & Clements, 1945). One may safely conclude, therefore, that platinum salts, whether carried as dust or mist, present an industrial hazard, and that such aerial contaminators should be carefully controlled.

7. Selenium

Selenium (Se) belongs to the same periodic group as sulphur and, like sulphur, it exists in a number of allotropic forms. It occurs in nature as selenides of lead, copper, mercury and silver.

Garlicky breath is a characteristic effect of the absorption of selenium. In fact selenium was discovered by Berzelius in 1817 in Gripsholm, Sweden, when his housekeeper complained that he was eating too much garlic, whereas he had been examining a selenium-bearing deposit formed in a sulphuric acid chamber. The volatile compound exhaled in the breath is probably dimethyl selenide $(CH_3)_2Se$. The amount of selenium which must be absorbed before a garlicky odour appears in the breath is greater than is the case with tellurium. The unpleasant odour also occurs in the sweat, the urine, and the faeces.

Selenium compounds are sometimes added to non-odorous, poisonous commercial gases such as methyl chloride and carbon monoxide, so that their stench will act as a warning. For this reason they are known as "stenching agents". Selenium is one of the substances employed by glassware manufacturers to produce various shades of red. Selenium compounds are used to supplement sulphur as a vulcanizing agent in the production of hard durable rubber.

The electrical conductivity of the grey form of selenium is poor but is greatly increased on exposure to light. This property makes possible all the fascinating uses to which the selenium cell is put. When an object intercepts a beam of light shining on a selenium cell, a change in electrical

resistance occurs and is instantaneously registered. The selenium cell makes it possible to transmit photographs and sketches along a wire (e.g. for newspaper illustrations), to make synchronous records of sounds and moving pictures for cinemas, and to construct street lamps, buoys and electric signs which light themselves up at dusk and extinguish themselves automatically at dawn. It is also used for burglar alarms and for opening and closing doors without touching them, to enable the blind to read ordinary type by ear by means of the optophone, and to register precisely the moment at which a runner touches the tape or a racehorse passes the finishing post.

a. Selenium in Soils

Selenium poisoning in animals was formerly called "alkali disease", because farmers associated it with alkali seeps and waters of high salt content. It was first described in 1856 in horses, by Madison, an army surgeon stationed at Fort Randall, in what is now South Dakota, USA. It has also been reported from the States of North Dakota, Montana, Wyoming, Kansas, Nebraska, Colorado and New Mexico. It does not occur in Great Britain, but the disease of livestock known in Ireland as "dry murrain" is evidently the same condition. The symptoms in livestock were not definitely ascribed to the consumption of selenium-contaminated grain until the relationship was demonstrated by Franke in 1934. The animals affected are horses, cattle, sheep, pigs and chickens. Soils which have been derived from certain geological formations contain selenium which is absorbed by plants to the extent that they are toxic when consumed by animals. The poisonous vegetation causes considerable livestock losses and is directly and indirectly a danger to health in certain areas. The selenium in contaminated cereals is associated with the proteins of the cereals. It is an integral part of the protein molecule and consequently there has been much speculation regarding the possibility of selenium replacing sulphur in cystine and methionine. Such substitution for sulphur in the sulphur-containing amino-acids of proteins affords a possible explanation of the poisoning of animals, for they show focal necroses of the liver in acute forms of the disease, and cirrhosis of the liver in chronic poisoning.

Acutely poisoned animals are found in parts of Wyoming where plants may contain selenium up to several thousand parts per million. The acute illness is called "blind staggers." In the early stages the animal may stray from the herd because of impairment of vision and difficulty in judging nearness of the objects in its path. Later the blindness increases and there is profuse lachrymation with oedema of the eyelids. There is also a perverted appetite with a desire to chew wood, bone, and even metal objects. The tendency to wander increases and weakness of the limbs occurs, but there is no involvement of the hoofs. There is evidence of abdominal pain, and death results from respiratory failure.

The chronic type, "alkali disease", is predominant in South Dakota where the vegetation, grains and forages contain up to 25 p.p.m. of selenium. Lack of vitality and loss of hair from the mane and tail are the first symptoms. There may be stunting of growth and inability to reproduce. The hoof elongates and assumes shapes so bizarre that animals often have to graze on their knees. It has been suggested that this deformity results from the replacement of sulphur, which is present in high concentration in the hoof, by selenium. Because of erosion of the growing ends of the long bones of the limbs the animals become stiff and lame. Death ensues from anaemia and emaciation. Sometimes sheep grazing over seleniferous areas produce lambs with abnormal eyes and deformed feet. In affected chickens the eggs are either sterile, or they produce a high percentage of monstrosities (Moxon & Rhian, 1943).

Many of the inhabitants of the highly seleniferous areas of South Dakota and Nebraska show gastrointestinal symptoms, believed to be associated with the ingestion of selenium contained in meat, eggs, milk and vegetables. Urinary analyses showed that many persons in the affected areas of these two States excreted from 20 to 198 μg. of selenium per 100 cm.[3] (Smith & Westfall, 1937).

b. Selenium in Industry

Where workers are exposed to finely divided selenium, the dust of the metal tends to collect in the upper nasal passages where it may cause anosmia, catarrh and epistaxis. In workers exposed to selenium dioxide Pringle (1942) reported dermatitis and paronychia. He found that the fingers, teeth and hair may become stained red from the precipitation of minute amounts of amorphous selenium in the tissues.

Clinton (1947) reported an incident in which a group of workers engaged in smelting scrap metal were suddenly and unexpectedly exposed to high concentrations of selenium fume. When the dross from the furnace was stirred up a cloud of reddish fume arose from the material and billowed up around the hood to the roof where it spread out and then gradually settled to the ground. The fume was intensely irritating to the eyes, nose and throat, and the works' chemist was notified at once. He immediately ordered the premises to be evacuated until the fume had dispersed. Fortunately no worker was exposed for more than two minutes. The fume disappeared in about 30 minutes, leaving reddish streaks on the floor about the furnace. In the afternoon of the same day the melt in the furnace was poured into ingots without incident. All exposed workers noticed immediate and intense irritation of the eyes, nose and throat, and an unpleasant sour garlic-like odour in the fume. The more heavily exposed workers complained of a severe burning sensation in the nostrils, "like a hot poker", a dryness of the throat, followed after about two hours by severe headache, mainly frontal, lasting until the following day. Several men noticed immediate sneezing, coughing and headache, followed for some hours by nasal congestion, dizziness and redness of the eyes. Most of them noticed an unpleasant taste in the mouth, and a similar odour of the skin and clothing. All of them recovered within three days; there were no sequelae.

Hydrogen selenide is particularly liable to cause laboratory accidents, though fatal ones are rare. Both Berzelius in Gripsholm and Professor P. Bruylants of Louvain University were overcome while handling this gas. It causes extraordinary and persistent irritation of the mucous membranes lasting for about 15 days. Bruylants lost his sense of smell almost completely during a period of more than four weeks. In 1947 Buchan reported five cases of industrial selenosis due to less than 0.2 p.p.m. of hydrogen selenide in the atmosphere. The men were handling an etching ink containing selenium and the penetrating putrid odour of hydrogen selenide was detectable at the etching machine. The predominating symptoms were nausea, vomiting, metallic taste in the mouth, garlic odour of the breath, dizziness and extreme lassitude.

Selenium compounds were detected in the urine. Clinical recovery occurred when a harmless etching ink was substituted for that containing selenium compounds.

c. Prevention

Workers exposed to selenium compounds should be given ascorbic acid daily in doses of 10 mg. per kg. body-weight. Such treatment aims at removing the garlicky odour from the breath and often succeeds. In workshops where selenium and its compounds are handled, all dust should be properly removed by exhaust ventilation, and suitable protective clothing worn as necessary. It is sometimes essential for the workman to wear a helmet with positive air-pressure. Suitable washing facilities should be provided and no food should be consumed in the shop. The disposal of surplus selenium compounds is a difficult problem. Burning cannot be carried out in a residential area, because the smoke has an obnoxious and persistent smell. If the material is merely dumped and allowed to drain into streams, there is the obvious danger of creating seleniferous areas. In theory, it would seem most satisfactory to reclaim the selenium for further use (Amor & Pringle, 1945).

8. Tellurium

Tellurium (Te) has been known since 1782. It belongs to the same periodic group as sulphur and is therefore similar to sulphur in its general chemical behaviour. It is now obtained mainly as a by-product of the electrolytic refining of copper. As small a quantity as 0.05% of tellurium added to lead effects profound changes in the physical properties of this metal, the grain structure produced being extremely fine and uniform. Tellurium-lead has good mechanical properties, its tensile strength when fully toughened being twice that of ordinary lead. Its greater toughness enables sheets to be bent double and hammered flat without fracture. Compared with ordinary lead, tellurium-lead pipes have twice the resistance to bursting by frost. When added either to stainless steel or to copper, tellurium gives improved machining properties. Tellurium compounds are employed to supplement sulphur as a vulcanizing agent in the production of hard durable rubber. Used in the making of machine belting they give improved flexion and oil resistance, as well as increased tensile abrasion resistance.

Much smaller quantities of tellurium compounds are needed to produce a garlicky odour in the breath than is the case with selenium. Gmelin (1824) was the first to observe the presence of this odour in the breath of animals after administration of inorganic compounds of tellurium. In 1884 Reisert gave men 0.5 μg. of tellurium dioxide by mouth and showed that they had garlicky odour of the breath in one hour and a quarter; this lasted 30 hours. Ingestion of 15 mg. produced a garlicky odour still obvious after 237 days.

De Meio (1947) studied the rate of appearance of garlicky breath after oral administration of a sodium tellurite solution, in a group of 13 men and 7 women. Although in some cases garlicky breath appeared in 20 to 30 minutes, with an intake of 1 μg. of tellurium, as sodium tellurite, in others it was necessary to increase the dose to 10, 25 and even 50 μg., to obtain the same effect. This difference in behaviour was not related to body-weight or sex. From the beginning of his work with tellurium De Meio became convinced that a much larger dose of elementary tellurium than of tellurite was necessary to produce the garlicky breath in rabbits. He thought that by reducing tellurite to elementary tellurium he could probably eliminate the garlicky breath. He chose ascorbic acid for the purpose because, at room temperature, it reduces tellurite to elementary tellurium (Levine, 1936). Ascorbic acid probably acts by reducing tellurite, tellurous acid and possibly other tellurium compounds to elementary tellurium, thereby decreasing the formation of dimethyl telluride, $(CH_3)_2Te$, the compound responsible for the garlic-like odour.

Chemists and workmen who suffer from the remarkably objectionable tellurium breath complain that when they travel in a motor-bus passengers who sit next to them get up and choose a seat at a distance. Their wives will not sleep with them nor kiss them. Laboratory technicians handling sodium tellurite as a medium on which to grow diphtheria bacilli may develop the garlicky breath. In 1920 several men were poisoned by fume in silver refining. A garlicky odour was noticed both in the breath and in the urine. There was dry mouth and skin, somnolence, anorexia and vomiting.

In 1946 a tragedy affecting three soldiers, of whom two died, was recorded by Keall, Martin & Tunbridge. In some army supplies certain bottles had lost their labels and had evidently been wrongly re-labelled. This led to retrograde pyelograms being done with sodium tellurite instead of sodium iodide. The soldiers had garlicky breath, renal pain, cyanosis, vomiting, stupor going on to coma, and two of them died within six hours. The amount of sodium tellurite used was approximately 2 g.

De Meio (1947) found that in two cases out of three, the garlicky breath disappeared following the administration of ascorbic acid in doses of 10 mg. per kg. body-weight. Four workers exposed to tellurium dust and suffering constantly from garlicky breath were given 750 mg. of ascorbic acid, three times daily at three-hourly intervals, and the garlicky breath either was considerably reduced in strength or completely disappeared; it returned, however, after treatment with ascorbic acid was stopped.

In workers exposed to tellurium compounds a daily dose of 10 mg. of ascorbic acid per kg. body-weight is usually enough to abolish the garlicky odour of the breath. Amdur (1947) described the accidental exposure of three metallurgists to tellurium fume for ten minutes while melting and pouring an alloy of 50 % tellurium and 50 % copper. Garlicky breath and sweat appeared within a few hours of the accident and next day all the men had become social outcasts even within their own homes. They were treated with a course of injections of 2 : 3-dimercaptopropanol (BAL). In spite of the fact that treatment did not begin until 48 hours after the accident they lost all trace of the garlic-like odour in 11 to 14 days after their common exposure.

9. Uranium

Uranium (U) is a hard, heavy, nickel-white metal. Ordinary uranium is radioactive and four isotopes are known; that of atomic weight 235 has been utilized in the so-called atomic bomb. The common non-military uses of uranium include its application as a colouring material in ceramics, as well as its use in photographic chemicals and as a catalytic agent.

Uranium and its salts are highly toxic. Numerous studies of uranium nephritis in animals have been made since Leconte (1854) first showed that absorption of small amounts over long periods of time caused chronic nephritis. MacNider

(1936) has shown that in dogs poisoned with uranium, hepatic degeneration occurs, although sometimes the animal can recover from the hepatic injury. Dogs receiving sodium citrate can survive an otherwise lethal dose of uranyl nitrate, because such treatment facilitates the excretion of uranium in the urine (Gustafson, Koletsky & Free, 1944). Uranium poisoning in man is rare. Workers handling it must be under constant supervision and, since it is a radioactive element, repeated blood counts must be taken. If a worker is excreting uranium in the urine, it can be detected in extremely minute amounts. Uranium hexafluoride fumes on exposure to air and is highly corrosive to glass and metal. Inhalation of the fume must therefore be strictly avoided (Fairhall, 1946).

10. Vanadium

The ores of vanadium (V) are patronite, vanadium sulphide, carnotite, potassium uranyl vanadate, and vanadinite, a lead vanadium oxide. In countries where the ores are not found, petroleum residues form the main source of supply. More than 20 tons of vanadium pentoxide are recovered annually from soot which collects in the boilers and smokestacks of ships burning Venezuelan and Mexican fuel oil. About 95% of the world's supply of vanadium is consumed in the manufacture of special alloy steels. Vanadium pentoxide is used as an oxidizing catalyst in the conversion of naphthalene to phthalic anhydride and is replacing platinized asbestos in the contact process for the manufacture of sulphuric acid.

In 1911 Dutton described vanadium poisoning in a factory where vanadium ore was ground. The clinical picture as he recorded it has never been confirmed. It included loss of appetite, anaemia, emaciation, diarrhoea, dimness of vision, melancholia, dry paroxysmal cough, haemoptysis and albuminuria. Vanadium was found in the urine, faeces and saliva. Dutton thought that pulmonary tuberculosis was apt to supervene upon the bronchitis caused by vanadium. In 1938 Molfino showed that vanadium anhydride has a strongly irritant action on the respiratory tract of animals. It is absorbed, and is excreted in the urine. In 1939 Symanski made a study of 19 cases which occurred in a metallurgical works in Germany. He claimed that it is only the pentoxide of vanadium which produces a toxic dust. He observed severe conjunctivitis, often with suppuration. There was also chronic bronchitis, with a feeling of constriction in the chest, persistent cough, profuse expectoration, and sometimes haemoptysis.

Balestra & Molfino (1942) reported respiratory symptoms in labourers working over petroleum ash containing vanadium. Wyers (1946) described 10 cases of respiratory disease among 90 workers making vanadium pentoxide. These men had complained of shortness of breath, pain in the chest, palpitation on exertion, and paroxysmal cough though rarely associated with haemoptysis. Examination showed greenish-black discoloration of the tongue, tremor of the fingers and arms, and rhonchi throughout both lungs. Three of them developed pneumonia, of which one died. Four showed dust reticulation in *x* rays of the lungs. Wyers concluded that colds and pneumonia were more frequent than in the general population but was not able to produce statistical evidence in support of this.

In order to prevent industrial poisoning by vanadium compounds, mechanization and enclosure of all dusty processes must be strictly enforced.

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SOME RESULTS OF EXPOSURE TO BERYLLIUM AND CHROMIUM

(FIGS. A—C)

Donald Hunter

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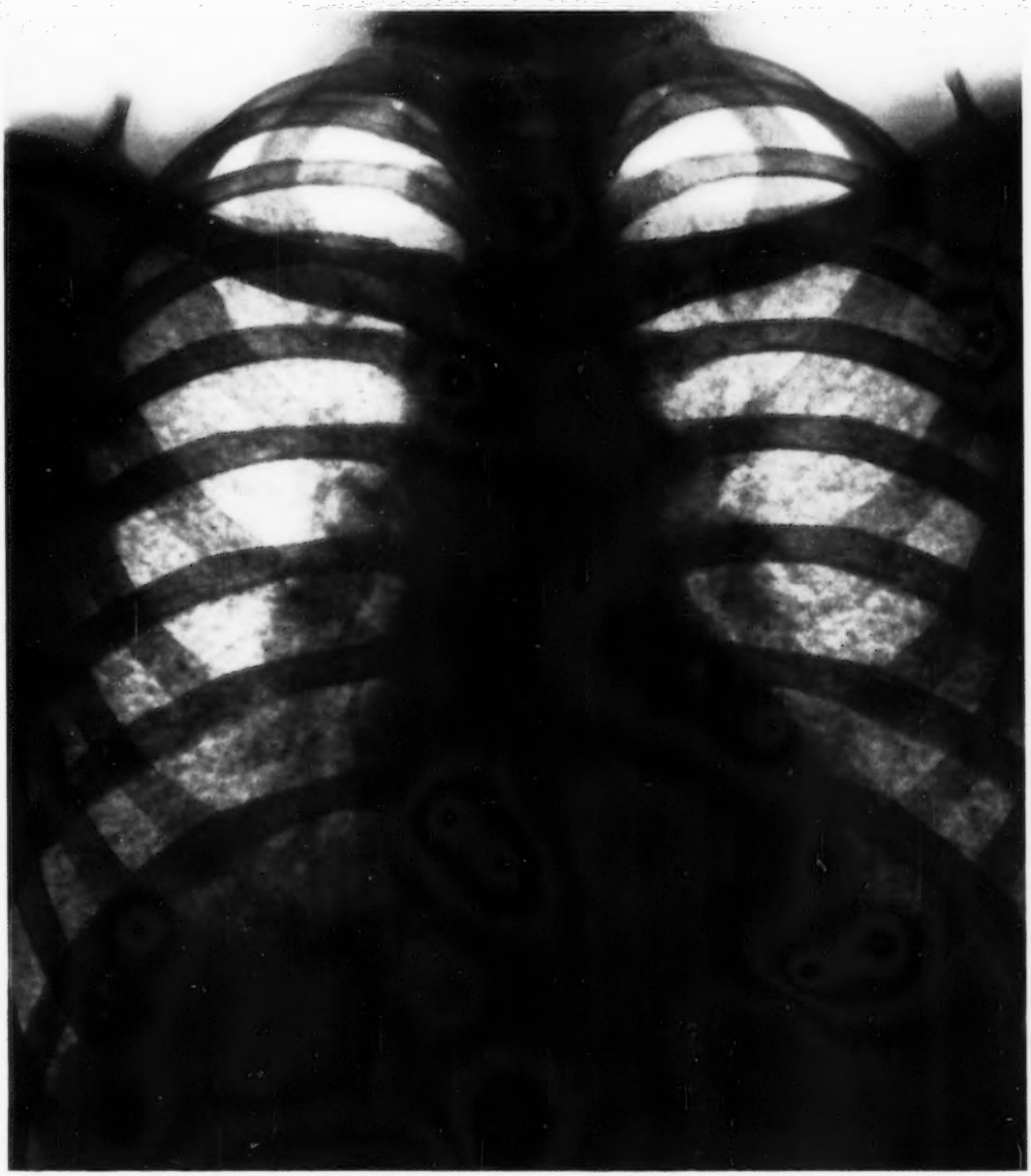

FIG. A. Chronic beryllium granulomatosis in the lungs of a woman, aged 24. She had been exposed to the dust of a phosphor for only two months. Dyspnoea began 10 months after exposure ceased

FIG. B. Subcutaneous beryllium granulomata in a boy aged 12, following a cut from a broken fluorescent lamp tube. (After Dr P. H. Nash, 1949)

FIG. C. Indolent ulcer, known as " chrome hole ", on the hand of a 46-year-old colour worker who had handled sodium bichromate for seven years

INDUSTRIAL DERMATITIS

(FIGS. D—L)

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FIG. D. Oil folliculitis of extensor aspect of elbow in a machine operator exposed to cutting oil

FIG. E. Hyperkeratosis on the arms of a machine operator exposed for 20 years to cutting oils

FIG. F. Acute vesiculation of fingers and hand caused by excessive use of cleansing agents

FIG. G. Papular rash in worker exposed to new alloy

FIG. H. Sensitivity to cetrimide dressing

FIG. J. Nummular eczema following exposure to chrome

FIG. K. Streptococcal infection of vesicular dermatitis

FIG. L. Cracking and fissuring of palm

NON-METALLIC TOXICOLOGICAL HAZARDS: SOME OF THE NEWER COMPOUNDS IN INDUSTRY

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A Silicon compounds
1 Ethyl silicates
2 Silicones
a Liquids
b Resins
c Rubbers
3 Other silicon compounds
B Fluorine compounds
4 Fluorinated paraffins
5 Tetrafluoroethylene
6 Fluorine
C Other compounds
7 Monomers
8 Ketene
References

The hazards of the better-known non-metallic compounds have been discussed on many occasions. New compounds are coming into prominence every year, and an attempt has been made here to discuss some of those which have recently become important and will probably be appearing in industry on a larger scale in the near future. No attempt has been made to deal with all of these substances, but a few of the most important are considered in this paper.

A. SILICON COMPOUNDS

1. Ethyl Silicates

In recent years the ethyl silicates have come into great prominence in industry owing to their property of slowly hydrolyzing and polymerizing to produce amorphous silica. It will readily be realized that a liquid which subsequently solidifies will have various applications, and these silicates are used for such diverse purposes as weatherproofing of buildings, for making moulds for stainless steel castings, and as constituents of paints and lacquers, etc. Their possible uses in other directions are being actively investigated. Ethyl silicates consist of mixtures of tetraethyl orthosilicate and various ethyl polysilicates and are used in various grades depending on the amount of polysilicates present. Tetraethyl orthosilicate is sometimes used free of any of the polysilicates, and it is an important constituent of all the grades of ethyl silicates. It would appear also to be the compound which gives rise to the chief hazard in the practical applications of these substances.

Tetraethyl orthosilicate is a colourless liquid and has an appreciable vapour pressure at ordinary temperatures, the vapour pressure at 20° C. being 1.8 mm. Although no toxic effects have been recorded during the industrial use of this compound, animal experiments have shown it to have considerable toxicity and it should certainly be used only when proper precautions can be taken. Experimental data have been recorded by Kasper, McCord & Frederick (1937), Smyth & Seaton (1940), and Rowe, Spencer & Bass (1948). All agree that, in rats, the vapours of this compound can give rise to very serious lung damage, consisting of oedema and haemorrhages. Inhalation of the vapour also led to the appearance of blood in the urine and post-mortem examination of animals killed by tetraethyl orthosilicate showed marked degeneration of the tubules of the kidneys. Some cloudy swelling was also found in the liver.

This compound in the vapour phase can act as an irritant to the eyes and nose but no permanent injury has been noted in the eyes of experimental animals, even when the liquid was instilled. This is in marked contrast to the effects of tetramethyl orthosilicate which is reported to cause necrosis of the cornea. There is no evidence that tetraethyl orthosilicate is

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TOXICOLOGICAL HAZARDS: METALS

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absorbed through the skin and it is definitely not a skin irritant. It can, however, remove the fats from the skin, as it is a fat solvent, and care should be taken to see that this property does not predispose personnel to dermatitis.

As a result of the experimental work on animals, Cook (1945) has suggested a maximum allowable concentration for tetraethyl orthosilicate of 100 parts per million (p.p.m.) by volume, and further recommends that all exposed personnel should be under medical supervision. It should be noted that such a concentration will be easily attained in the practical use of this compound.

The polysilicates are less volatile than tetraethyl orthosilicate and, although no direct information as to their toxicity is available, a dangerous concentration of vapour cannot arise so readily.

As far as is known at the present time these compounds have not given rise to silicosis.

2. Silicones

a. Liquids

These compounds are finding an increasing use in industry owing to their chemical inertness and their viscosity. As distinct from the silicates, the carbon and the silicon are directly attached and no ester linkage is found in the molecule. The silicones of commerce can be designated by the formula $(CH_3)_3$ Si—O—[Si$(CH_3)_2$—O]$_n$—Si$(CH_3)_3$. The viscosity of the compounds can be varied by varying "n", which can be increased to over 1,000. Although the methyl compounds are the ones in most common use, other organic groups can be substituted and the possible future developments will no doubt include a large variety of compounds. In fact, some compounds containing both methyl and phenyl groupings are being used as silicone resins.

These compounds (and also the resins) have been investigated by Rowe, Spencer & Bass (1948). The first member of the series is hexamethyl-disiloxane (i.e., n = 0); it is more like a solvent in its action and has a considerable vapour pressure (boiling-point = 99.5° C.). Its toxicity in the vapour phase is such that concentrations of the order of 4% by volume cause death to guinea-pigs within 20 minutes. There is not enough information available on chronic exposures to determine a maximum allowable concentration, but rats and guinea-pigs showed no chronic effects when exposed to 4,400 p.p.m. for 15 and 18 seven-hour exposures respectively. This substance is a temporary eye irritant and conjunctivitis in humans has been reported.

The higher silicones (n = 3 or more) are much less reactive than hexamethyl-disiloxane and would appear to have very few toxic properties as far as is known up to the present. They have no appreciable vapour pressure and are viscous fluids used as lubricants and transmission fluids. Fed to animals by the mouth they appear to act as completely inert bodies and as a result have a laxative effect similar to that of liquid paraffin. They are not skin irritants but in rabbits can cause slight eye irritation some time after being instilled into the eye.

b. Resins

The silicone resins are similar to the liquids, but some "cross-linkage" has occurred in the molecule, i.e., the silicone chain is attached to one or more silicone chains by another Si—O—Si linkage. These compounds can be of the methyl polysiloxane type or the methylphenyl polysiloxane type. Once again these compounds would appear to be quite inert, and no toxic effects have been reported when these resins were fed to guinea-pigs in amounts up to 3 g. per kg. body-weight.

An interesting use of some of these resins is as pan glazes in the baking of bread. By using these materials it has been possible, because of the water repellent action of the glaze, to dispense with the use of grease round the baking tin. The question of absorption of the resin by the bread and the possibility of toxic effects have been investigated by Coppock, Hulse & Urie (1949). They have shown that the absorption of the silicone into the bread is very low indeed and at a maximum would be represented by less than 0.5 p.p.m. of silica. Rowe, Spencer & Bass (1948) carried out prolonged feeding experiments on rats with the heat-treated silicone pan glaze and found no effects whatsoever, even when the diets contained 3% of resin (the highest proportion tested). These series of experiments have not indicated any toxic effects from the use of silicone resins in the baking of bread.

c. Rubbers

These compounds are polymers of methyl siloxane $(CH_3)_2SiO$, but groupings other than CH_3 can also be utilized. They have properties of adhesion to glass, steel, etc., that make them of interest to the engineer. One adaptation, however, is of great interest. According to Doede & Panagrossi (1947) the properties of these "rubbers" make it possible to construct conveyor belts for use in the preparation of foodstuffs. The foods can be dehydrated on such a belt at a temperature of 225° C. It is claimed that the "rubbers" are odourless, tasteless and non-toxic and unaffected by water vapour or food fluids.

3. Other Silicon Compounds

The manufacture of the silicone involves the use of simpler silicon compounds, some of which give rise to serious toxic effects. The best-known of these compounds is silicon tetrachloride, which was once suggested as a war gas. Other derivatives of silicon tetrachloride known as the chlorsilanes are equally toxic; they are used in the manufacture of silicones. These compounds are of the type in which one or two chlorine atoms in silicon tetrachloride have been replaced by methyl or ethyl groups, e.g. dichlorodiethyl-silane, methyltrichloro-silane, etc. All of them are very easily decomposed by water, giving off hydrochloric acid, and as a result they are colourless fuming liquids. Rowe, Spencer & Bass (1948) have investigated these compounds and demonstrated their toxic properties. All of them are highly corrosive and give rise rapidly to severe burns on coming in contact with the skin. The effects of splashes in the eye are very severe and these compounds should not be used unless the eyes are completely protected. Any splashes on the skin or in the eyes should be immediately treated by copious douching with water, which must be readily available in any factory where these materials are handled.

The vapours of these compounds, consisting in part of hydrochloric acid, are also highly irritant to the eyes and the nose. Like all such vapours, they can cause severe lung damage and personnel should avoid breathing them. There is no information as yet on which to base a maximum allowable concentration.

The other class of compounds which are intermediates in the manufacture of silicones is the "ethoxysilanes". These are compounds in which the hydrogen atoms of silane (SiH_4) have been replaced by at least one ethoxy group plus other alkyl groups. They are all ethereal liquids. The best-known member of the series is tetraethyl orthosilicate or tetraethoxysilane and it has already been dealt with above. Other members of the series such as methyl triethoxysilane and diethoxy dimethylsilane would appear to be less acutely toxic than tetraethyl orthosilicate. Little is known of the chronic effects of these compounds and at present it would seem the safest course to use the same precautions with them as with tetraethyl orthosilicate.

It should be noted that in Great Britain no canister gas-mask for protection against these volatile silicon compounds has had official approval. If protection from vapours becomes necessary, self-contained or long-distance breathing apparatus should be made available.

B. FLUORINE COMPOUNDS

During the last few years there has been much activity in the field of fluorine chemistry and many organic fluorine compounds have been prepared and their properties examined. As a result, quite a number of organic fluorine compounds have been introduced into industry and undoubtedly more will become available in the near future. There is also considerable activity in the inorganic field of fluorine chemistry.

4. Fluorinated Paraffins

The best-known organic fluorine compound is the refrigerant, dichlorodifluoromethane; its trade name in Great Britain is "Arcton 6"; it is made in the USA under the name of "Freon 12". It is a colourless, odourless gas and has practically no toxic effects. It should be pointed out, however, that, although its toxicity is very low, it does not act completely as an inert gas and in very high concentrations can produce some toxic effects. When animals are exposed to concentrations of 20% by volume some narcotic effects are produced (Midgley & Henne, 1930; Brenner, 1937), but no chronic effects have been reported. A concentration of 10% (100,000 p.p.m.) is generally reckoned as perfectly safe for prolonged exposures.

Some of the other members of the fluorinated paraffin series have shown themselves to be remarkably inert and to have toxic properties much lower than the corresponding chlorine derivatives: such are dichloromonofluoromethane where the maximum allowable concentration has been proposed as 5,000 p.p.m., and difluoromonochloromethane where the maximum allowable concentration has been suggested as 20,000 p.p.m. Both these compounds are colourless gases and have been used as refrigerants. Difluoromonochloromethane, however, is the basic material for the preparation of tetrafluoroethylene and its polymers.

Whilst many of the fluorine derivatives of methane, chlormethane, ethane and chlorethane are much less toxic than the corresponding chlorine compound, it should not be assumed without evidence that this is always so. The toxicity of tetrachlorotetrafluoropropane, for example, is stated to be extremely high and 16 p.p.m. can cause death in experimental rats (Carpenter, Smyth & Pozzani, 1949). It will also be appreciated that any compound which can give hydrofluoric acid on decomposition may become, in fact, highly dangerous although the pure compound is of low toxicity.

All the fluorinated methanes and ethanes can give rise to hydrofluoric acid or other poisonous fluorine compounds when brought into contact with a naked flame, and dangerous concentrations of such gases are easily set up. In using these materials care must be taken to avoid such incidents. It is peculiarly difficult in practice to ensure that the atmosphere of a plant is free from these compounds as, owing to their inert and odourless nature, high concentrations can be present without any noticeable signs.

5. Tetrafluoroethylene

By the pyrolysis of difluoromonochloromethane a complex mixture of fluorinated hydrocarbons is obtained. The most important of these is tetrafluoroethylene, which can be polymerized to give polytetrafluoroethylene; this polymer is of great commercial importance. The process is being developed on a large scale and is one of the most important in the field of fluorine chemicals.

Unfortunately little accurate information is available as to the concentrations of tetrafluoroethylene which might give rise to toxic effects. Park *et al.* (1947) give some qualitative data on the toxicity of the compounds produced by the pyrolysis of difluoromonochloromethane. Tetrafluoroethylene, which is a colourless gas, is stated to be relatively non-toxic and many others of the pyrolysis products are evidently of low acute toxicity. However, some of the pyrolysis products are in fact highly toxic although no toxic concentrations are mentioned. These compounds are thought to be fluorinated derivatives of methyl cyclohexane and they have to be carefully removed from the tetrafluoroethylene.

6. Fluorine

One of the reasons why the fluorine compounds can be developed to such an extent is that elementary fluorine is now available commercially, and distribution and use have now been worked out. It will be realized that such a dangerous gas can be used only under special conditions. No information is available to determine the maximum allowable concentration, but this must be very low indeed. Even assuming that it is immediately transformed into hydrofluoric acid, then the concentration cannot be more than 1 p.p.m., as each molecule of fluorine produces 2 molecules of the acid, and 2 to 3 p.p.m. is the maximum allowable concentration for hydrofluoric acid. Fluorine gas can cause burns in the skin similar to those caused by liquid hydrofluoric acid and they should be treated in very much the same way.

C. OTHER COMPOUNDS

7. Monomers

The development of new plastic materials is bringing into the chemical industry many new compounds besides those mentioned under silicon and fluorine. The methacrylate monomers are methyl methacrylate and butyl methacrylate. These compounds are both esters and, like most esters, have narcotic properties. They do not, however, present any special problems other than those of narcosis and inflammability.

The methyl and ethyl acrylates are now being developed and these two compounds are much more toxic than the methacrylate. They are much more irritant than the methacrylates but neither series of compounds has shown any evidence of having cumulative action. Treon, Sigmon, Wright & Kitzmiller (1949) found that rats could be killed by concentrations of 237 p.p.m. of methyl acrylate and 272 p.p.m. of ethyl acrylate. Lower concentrations can give rise to some irritation and it is obvious that the maximum allowable concentration will be very low. Both compounds can cause irritation to the skin and eyes.

Another toxic compound which is being used as the starting-point of polymers is acrylonitrile. This compound, which is a colourless liquid, has a low boiling-point and toxic concentrations can easily arise. It has been investigated by Dudley & Neal (1942) and shown to be highly toxic, the effects being those of a typical nitrile. There is also the possibility that it may damage the kidney in both acute and chronic exposure. The suggested maximum allowable concentration is 20 p.p.m. and this number has been given statutory force in certain States of the USA.

8. Ketene

This is a colourless gas now being used as the starting-point in organic syntheses. It is extremely reactive and highly toxic. Its properties in many ways resemble those of phosgene, the chief danger arising from absorption of it being lung oedema. The work of Treon *et al.* (1949) shows that some irritant effects are obtained in the lungs after intermittent inhalation of only 1 p.p.m. A suitable canister respirator for use against this compound has been approved by H.M. Chief Inspector of Factories.

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INDUSTRIAL SOLVENTS: THE AROMATIC AND CYCLIC HYDROCARBONS

A Review of their Properties, Industrial Uses, and Toxicology

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A The aromatic hydrocarbons
1 Benzene
2 Toluene
3 Xylene
4 Ethyl benzene
5 Cumene

B The cyclic hydrocarbons
6 Cyclohexane
7 Methyl cyclohexane
8 Tetralin
9 Decalin
10 Turpentine
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Among the almost unlimited number and increasing variety of industrial solvents, the aromatic and cyclic hydrocarbons are of primary importance in industry and toxicology. They are much used in industry because their solvent action is efficient and because they are relatively inexpensive and easily obtained. The aromatic hydrocarbons are of supreme importance in toxicology because the one most widely used, benzene, is among the most toxic of all industrial solvents, especially as a chronic poison.

As acute poisons, both groups are narcotics, acting upon the central nervous system, with a fatal effect if inhaled in high concentrations. As chronic poisons, the two groups differ in their points of action on the living organism, the aromatic hydrocarbons having an almost specific effect on the haemopoietic system, the cyclic group having very little.

A. THE AROMATIC HYDROCARBONS

The chief members of this group in use in industry are benzene, often, but incorrectly, called benzol, and its homologues toluene, xylene, and, of lesser importance, ethyl benzene and cumene. They are all good solvents for fats, oils, bitumens, many resins and copals, cellulose ethers, rubber and many polymers, and are therefore very widely used in a great number of industrial processes, such as fat extraction, the rubber industry, paint and varnish manufacture, dry cleaning, artificial leather making, and the numerous subsidiary processes depending on these.

1. Benzene

Benzene (C_6H_6), a coal tar derivative, must be carefully distinguished from benzine, which is a petroleum distillate of extremely variable chemical properties and composition, sometimes rich in aromatic hydrocarbons, sometimes consisting essentially of paraffins and cycloparaffins. The chronic toxic action of benzine resembles that of benzene only when its aromatic hydrocarbon content is very high.

The product most widely used, commercial 90% benzene, is a colourless mobile liquid with a not unpleasant odour; it is easily volatile, especially if heated, its time of volatilization relative to that of ether being 3:1. Its designation indicates that 90% by volume distils below 100° C.; the rest distils below 120° C. It is thus distinguished from pure benzene, which has a boiling-point of 80° C., and from "commercial crystallizable (100%)" benzene which has a boiling range of 80–81° C. and, like commercial 90%, also contains traces of xylene, toluene, phenol, carbon disulphide and many other substances.

Apart from its use in the production of benzene by the distillation of coal and coal tar, its use in the blending of motor fuels, and its handling in large quantities in closed systems in the chemical industries, benzene has an extremely wide field of application.

In the "rubber industry" alone it is used in many subsidiary processes, such as the manufacture of tyres, straw hats, cardboard boxes, waterproofed goods, boots and shoes, cameras, sealing of cans, etc. Its solvent action on fats also gives it great importance in removing grease, in the extraction of alkaloids and other substances, and, though not to so great an extent as formerly, in the cleaning and dyeing industry. Two other industries in which benzene has fortunately been largely superseded by less toxic substances are the photogravure printing process and the manufacture of paints and lacquers.

Acute and chronic benzene poisoning, as shown by the investigation of their manifestations both in human beings and in experimental animals, are entirely distinct entities. In acute benzene poisoning the toxic action is exerted on the central nervous system, first of a convulsive, neurotoxic character, later as an asphyxiating narcotic. Chronic benzene poisoning, on the other hand, attacks primarily and with great severity the haemopoietic system, producing not only the classical picture of aplastic anaemia described by the early workers in this field, but also wide variations of disturbance of the blood picture, ranging from hyperchromic anaemia of pernicious type to typical acute leukaemia. An unfortunate aspect of chronic benzene poisoning, from the point of view of preventive and curative measures, is the fact that symptoms frequently bear little or no relation to the severity of blood disturbance. In a case observed by the author, for example, blood examination revealed severe leucopenia and anaemia, which ultimately progressed to fatal aplastic anaemia, at a time when there was no complaint of disturbance of health.

Acute benzene poisoning. Although it has been stated (Hamilton & Johnstone, 1945) that "acute benzene poisoning is of little importance under modern industrial management," severe and even fatal cases do occur owing to unforeseen imperfection of plant or to neglect of adequate precautions, especially during the cleaning of tanks containing or having contained benzene. During the last seven years 51 such

cases, nine of them fatal, have been reported to the Factory Department of the Ministry of Labour.

In the most severe poisoning, following inhalation of large amounts of the vapour (200,000 p.p.m. may be fatal if inhaled for 5–10 minutes), convulsive movements, paralysis and unconsciousness with dilated and non-reacting pupils may be followed rapidly by death. In milder forms there is first a state of euphoria, followed by headache, giddiness, nausea, vomiting, staggering gait and inability to escape from the site of poisoning. Many of these cases recover with no serious after-effects, but sequelae, including dizziness, respiratory catarrh, nervous disorders, depression, sleep disturbance and exhaustion have been recorded.

Immediate removal from exposure, followed by artificial respiration and administration of oxygen and CO_2, are the recognized methods of treatment.

Chronic benzene poisoning. The most prominent early symptom is lassitude, especially noticeable in the evening. This may be the only complaint elicited from a group of workers whose blood picture shows, in a number of cases, changes due to what may be described as " benzene absorption " rather than true benzene poisoning. Other slight preliminary symptoms include headache, giddiness, loss of appetite, indigestion, nausea and even vomiting.

Among the later symptoms, which usually indicate severe and perhaps irreparable damage to the bone-marrow, are menorrhagia or metrorrhagia, epistaxis, bleeding from the gums, a purpuric eruption, and, more rarely, haemoptysis or haematemesis; these are accompanied by extreme pallor, weakness, dyspnoea, and a progressive deterioration in health.

It is now recognized that the variations from the classical blood picture of leucopenia, anaemia and thrombocytopenia can be explained by the fact that side by side with the destructive effect of benzene on the bone-marrow there evolves a regenerative activity. The resulting picture in any individual case is therefore a reflection of the balance of these opposing processes. The bone-marrow may exhibit areas of aplasia alternating with areas of hyperplasia (Jackson, Parker & Lemon, 1940; Bowers, 1947) and it is possible that the extreme evolution of the hyperplastic process may explain those cases which eventually die of acute leukaemia.

The commonest early change, in the author's experience of a very large number of cases (Paterson & Browning, 1944), is neutropenia, followed closely by leucopenia. This is quite frequently associated with a relatively slight fall in the total number of red cells, without a corresponding fall in haemoglobin value, so that the slight anaemia is associated with a high colour index. In some cases, however, anaemia of this nature is present in the very early stages, and leucopenia develops a little later.

Thrombocytopenia is also a frequent feature of chronic benzene poisoning and, according to Helmer (1944), a persistent one, remaining even when red cells, haemoglobin and leucocytes have returned to normal following removal from exposure.

Abnormality of the blood picture may persist for periods of several years after removal from exposure and after disappearance of all symptoms. This was so in a number of men, examined by the author in 1945, who had been severely affected by exposure to benzene used in a photogravure process. One of these, when first examined, had a total red cell count of 3.9 millions per $mm.^3$ and 3,425 total white cells; eight months later, though his anaemia had decreased, his total white cells remained at 3,400, although he had had no further exposure to benzene.

In severely affected cases, where purpura or other haemorrhagic symptoms have occurred, it appears practically impossible to save the life of the patient by any means. Repeated blood transfusions produce temporary improvement, as does the administration of pentnucleotide, liver extracts and iron, but unfortunately relapses are common. In less severe cases crude liver extract has the effect of raising the total number of neutrophils, and a vitamin-rich diet, including administration of vitamin C, has been recommended (Seyfried, 1942). The rationale of vitamin C treatment rests on the fact that workers exposed to benzene are said to show a decreased urinary excretion of the vitamin and increased consumption of foods containing vitamin C (Friemann, 1936; Meyer, 1937).

2. Toluene

Toluene (methylbenzene, $C_6H_5.CH_3$), like benzene, is produced from the distillation of coal tar. It is a colourless fluid with an odour rather similar to that of benzene. The boiling range of the commercial product is 109–111° C. It is less volatile than benzene, volatilization time relative to ether being 6.1 : 1. Its solvent properties resemble those of benzene, but it is more suitable than benzene for addition to solutions of cellulose esters in other solvents. It is used much less than benzene in the rubber industry but more as a diluent for lacquers and in colour-printing processes.

Although it is, like benzene, an acute narcotic, its chronic toxic effect is much less severe, especially with regard to the blood-forming organs. There is some evidence, however, that it may cause liver injury (though to a much smaller extent than some of the chlorinated hydrocarbons) and some nervous disturbance.

From animal experiments, toluene appears to be even more highly narcotic than benzene; severe acute poisoning in man is much rarer, and no fatal cases have been recorded. The chief symptoms are headache, nausea, giddiness and faintness; actual unconsciousness supervened in only two of the eight cases of acute intoxication reported to the Factory Department since 1940.

Until comparatively recently there has been a prevalent belief that toluene is a haemopoietic depressant of nearly as great a severity as benzene. From the results of a careful investigation on both men and animals by the United States Public Health Service (von Oettingen, Neal & Donahue, 1942) it appears that much of this belief has been based on reports of cases where the solvent used was commercial toluene containing up to 20% of benzene, and that the blood changes observed were therefore due to a " benzene effect", not to toluene itself. It is probable that the difference between the effect of toluene (and also xylene) and benzene on the haemopoietic system can be correlated with the difference in their metabolism in the organism, benzene being oxidized to highly toxic polyphenols, hydroquinone, etc., whereas toluene produces benzoic acid, later excreted as hippuric acid, and xylene is oxidized to toluric and toluic acid.

The chief symptoms of chronic toluene poisoning are related to the nervous and gastrointestinal systems. With concentrations of 50–100 p.p.m. the first effects are fatigue and mild headache; above 200 p.p.m. muscular incoordination may occur, and with 600–800 p.p.m. there may be

mental confusion, staggering gait and severe headache (von Oettingen *et al.* 1942). Gastrointestinal disturbance is shown by loss of appetite, nausea and vomiting; palpable enlargement of the liver has been recorded in a number of workers examined (Greenburg *et al.* 1942). However, this was not accompanied by any clinical or laboratory evidence of disease of the liver and it has been suggested, from analogy with animal experiments, that it is associated only with a change of density of the liver cells, perhaps due to endosmosis.

Very few investigators, other than Langelez, Peremans & Bastemer (1940), believe that toluene causes as much haemopoietic injury as benzene. Most of the cases with a blood depressant effect recorded have been found to have been exposed to commercial toluol containing up to 20% of benzene, and in the only fatal case recorded, that reported by Ferguson, Harvey & Hamilton (1933), these authorities have themselves admitted the possibility of idiopathic agranulocytic anaemia.

3. Xylene

Commercial xylene (dimethylbenzene, $C_6H_4(CH_3)_2$) is usually a mixture of three isomers, ortho-, meta-, and para-xylene, with the meta derivative predominating. It may also contain small amounts of toluene, ethylbenzene and pseudocumene. The boiling-points of the three isomers are: ortho- 142.3° C., meta- 139° C. and para- 138° C. The boiling range of commercial xylene is between 135 and 145° C.; its specific gravity is 0.862–0.865. Its solvent properties are similar to those of xylene.

It is a colourless liquid with a strong smell and is used in much the same way as toluene, especially in photogravure and the quartz crystal industry. Although it is an acute narcotic of about the same potency as toluene its long-term effects on the haemopoietic system are certainly much less than those of benzene and probably less than those of toluene. Experiments on animals show that xylene has a higher acute toxicity than benzene and about the same toxicity as toluene, but fatal cases in man from inhalation of pure xylene have not been recorded. Non-fatal cases show symptoms characteristic of giddiness from nerve poisoning, and even unconsciousness.

Where nervous symptoms of any considerable severity following long-continued exposure to xylene have been reported, as in the investigation by Brachmann (1937) of intaglio printers, it has usually been found that the solvent was not pure xylene but a mixture of commercial xylene and toluene or other solvents. In a large series of cases among photogravure printers investigated by the author in 1945–1947 (unpublished observations) the chief symptoms complained of were sleepiness, headache and lassitude; giddiness was very rare.

There is no doubt that xylene, unlike benzene, is relatively innocuous to the haemopoietic system, especially with regard to the causation of aplastic anaemia. In the author's experience the characteristic severe and depressive " benzene effect " on the bone-marrow has been completely absent in all workers examined after they had been working with pure xylene as the solvent.

4. Ethyl Benzene

Ethyl benzene (phenyl ether, $C_6H_5C_2H_5$) is obtained by the ethylation of benzene. It is a colourless liquid with a boiling-point of 136.5° C., a specific gravity of 0.87 and a flash-point of 15° C. It is insoluble in water but soluble in alcohol and ether. In industry, its chief use is as a diluent for lacquers; it has been suggested as an addition to motor fuel as an " anti-knock " agent.

As an acute narcotic ethyl benzene appears to be slightly more toxic than benzene, since, in animals, prostration and death occur at slightly lower concentrations than with benzene (Lehmann & Flury, 1943). It has a marked irritative effect on the skin and eyes and is mildly irritant to the lungs. Death is caused chiefly by injury to the central nervous system (Yant *et al.* 1930). No investigations of its chronic toxic effects have been made and there have been no reports of systemic injury from its industrial use. According to Oettel (1936) ethyl benzene is the most severe skin irritant of the benzene series and its irritant effect on the eyes begins at about 200 p.p.m., becoming severe at 1,000 p.p.m. and intolerable at 5,000 p.p.m. (Patty, 1949).

5. Cumene

Cumene (isopropyl benzene, $C_6H_5.CH(CH_3)_2$) is one of the higher homologues of benzene. The pure product can be prepared synthetically, but the technical product obtained during the fractionation of petroleum is usually at least 95% pure. It is insoluble in water but soluble in ethyl alcohol and ethyl ether. Pure cumene has a boiling range of 151 to 152.5° C. Its specific gravity at 25° C. is 0.837. The technical product has a boiling range of 151 to 156.2° C. (Ward & Kurtz, 1938). It is used in organic synthesis and, though not extensively, as a constituent of lacquer solvents. It is a potent narcotic of slow induction and long duration, but since its volatility is relatively low it should be easily controllable as an industrial hazard. Its slow elimination suggests the possibility of a cumulative effect, but so far none has been reported in human beings. The narcosis induced in animals from inhalation of cumene is entirely depressant, with no initial stimulation such as occurs with benzene and toluene; narcosis develops more slowly, lasts longer, and the lethal dose is less (10 mg./l. air according to Werner, Dunn & von Oettingen, 1944). However, comparison on the basis of their relative saturation concentrations shows that its " hazard index " is 4, that of toluene is 10, and that of benzene, 12.

Continuous exposure to non-lethal doses of cumene vapour causes fatty changes in the livers and kidneys of animals, more severe than benzene and about the same as toluene. No toxic effects in human beings have been reported.

B. THE CYCLIC HYDROCARBONS

6. Cyclohexane

Cyclohexane (hexamethylene, hexahydrobenzene, C_6H_{12}) occurs in Caucasian petroleum and is manufactured by the hydrogenation of benzene. It is a colourless mobile liquid with a somewhat pungent smell. Its boiling-point is 51° C. and its specific gravity 0.74. It is a good solvent for rubber, bitumen, and paraffin wax. In industry it is used as a grease remover, a solvent for rubber, and a paint thinner.

In high concentrations cyclohexane is a powerful narcotic. There is some discrepancy among the results of animal experiments as to whether it is convulsant as well as paralytic, but the most recent investigations (Treon, Crutchfield &

Kitzmuller, 1943) show that inhalation of concentrations of 1.26% and above do cause spasmodic convulsions.

From the point of view of chronic toxicity it is undoubtedly a much safer solvent than benzene, since it has no effect on the haemopoietic system. Only slight degenerative changes in the liver and kidneys were found after prolonged and repeated exposure, the pathological changes in the tissues generally being non-specific and characteristic of acute toxic reactions. Irritation of the skin followed cutaneous application.

There is no record of toxic effects in man but Treon *et al.* (1943) have said that a temporary decrease in the inorganic sulphate content of the urine and a temporary increase in the glucuronic acid should be a useful measure of the absorption of cyclohexane. It has been suggested that the maximum concentration allowed in the atmosphere should be 300–400 p.p.m.

7. Methyl Cyclohexane

Methyl cyclohexane (hexahydrotoluol or heptanaphthene, $C_6H_{11}CH_3$) is present in the distillate of certain petroleums, and is produced by the catalytic reduction of toluene or by the reaction of benzene with methane. It is a colourless liquid with industrial uses similar to those of cyclohexane. Its boiling-point is 101.2° C. and its specific gravity 0.733.

Methyl cyclohexane is, from the results of animal experiments, a narcotic of higher toxicity than cyclohexane, causing convulsions when high concentrations are inhaled. Its chronic toxicity appears to be less, since repeated exposure to 1,162 p.p.m. proved safe for rabbits, whereas slight damage to liver and kidneys appeared with 786 p.p.m. of cyclohexane. No haemopoietic injury was observed (Treon, Crutchfield & Kitzmuller, 1943).

No toxic effects in man have been reported. The maximum permissible concentration suggested by Cook (1945) is 1,000 p.p.m., but Patty (1949) suggests that even though permanent damage would not be expected at concentrations up to 800 p.p.m., for prolonged exposure 500 p.p.m. should not at present be exceeded.

8. Tetralin

Tetralin (tetrahydronaphthalene, $C_{10}H_{12}$) is a colourless liquid formed by the hydrogenation of naphthalene, with a smell resembling that of naphthalene. It is only slightly volatile. "Tetralin Extra" is a mixture of tetralin and decalin, with a more powerful solvent action than either alone. It is used in industry as a constituent of floor and shoe polishes, a paint remover and paint thinner, a rubber solvent, and as a fumigant for moths.

The principal effect of exposure to tetralin is the appearance of a green coloration of the urine which, in man, does not appear to be associated with injury to the kidneys, but to be due to transformation products formed during digestive processes. In animals, however, the most recent investigations, by Cardani (1942), show that definite injury to the liver and kidneys can be produced both by ingestion and long-continued inhalation of tetralin. For this reason observers such as Röckemann (1922) have advised caution in employing workers who may be suffering from any disorder of the kidneys, in processes involving the use of tetralin.

Skin lesions, of an eczematous nature, and irritation of the eyes, nose, and throat, have been recorded in workers who have had prolonged contact with tetralin (Cardani, 1942). Headache, nausea, vomiting and drowsiness have been recorded in a few cases (Koelsch, 1926), but in this country and in the USA no severe symptoms have occurred.

9. Decalin

Decalin (decahydronaphthalene, $C_{10}H_{18}$) is very similar in properties and industrial uses to tetralin but has a lower boiling-point (189–191° C.), a slightly higher volatility, and a slightly less powerful solvent action.

While animal experiments show that decalin has an action on the kidneys similar to that of tetralin, it does not produce the green coloration of the urine. One case of possible kidney involvement in a worker employed in cleaning paving stones with decalin (Cardani, 1942) and several cases of eczema among painters (Koelsch, 1926) have been reported.

10. Turpentine

Turpentine ($C_{10}H_{10}$) or "gum spirit" is a volatile oil obtained from various species of pine and containing a mixture of terpenes; the pure "gum spirit" produced by tapping the living tree is composed almost exclusively of α-pinene; "wood turpentines" produced by destructive distillation of wood contain methyl alcohol, formaldehyde, phenols, pyridines, etc., and are considered by McCord (1926) to be responsible for the well-known "turpentine dermatitis".

Turpentine is a good solvent for many substances, particularly fats, resins and rubber. Its specific gravity is 0.863 to 0.875 and its boiling range is 155 to 180° C.

It has many uses—in the paint industry, in the manufacture of cleaning polishes, as a cleaner in the printing industry, in oil extraction, in the synthesis of camphor, and in the rubber industry.

Turpentine, especially wood turpentine (McCord, 1926) is irritating to the skin and may cause severe dermatitis. Irritation of the nose, throat and eyes from inhalation of the vapour occurs at atmospheric concentrations of less than 1 mg. per litre (Nelson *et al.* 1943). Injury to the kidneys, in the form of acute glomerulonephritis, has been recorded following severe exposure (Chapman, 1941; Wilks, 1930) but this condition appears to clear up completely on removal from exposure. The urine of exposed persons has an odour of violets, due, it is believed, to the combination of some of the turpentine excreted with glucuronic acid.

The question of chronic turpentine poisoning, possibly leading to Bright's disease, has given rise to much controversy; the conclusions of the enquiries of the Departmental Committee on the Use of Lead in Painting in 1923 did not confirm the assumption that turpentine was the cause of Bright's disease in painters, and a more recent review by Chapman (1941) is in agreement with these conclusions.

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HEALTH HAZARDS FROM INSECTICIDES

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1 General nature of the hazards
2 Toxic properties of certain typical insecticides
a Tetraethyl pyrophosphate and parathion
b Pyrophosphoric tetrakis dimethylamide
c 3 : 5 Dinitro-orthocresol
d Dichlorophenyl-trichlorethane and benzene hexachloride
3 Conclusions
References

This article contains a brief review of the health hazards that may be encountered as a result of the increasing use of synthetic insecticides for the treatment of growing crops and stored food products. The need to improve food production in the British Isles has encouraged the use of these compounds in normal agricultural practice. At the same time an ever increasing number of compounds with insecticidal properties is being produced, and there is a tendency to exploit them before adequate information is available about their toxic properties towards mammals, including man.

A general outline of the problem will be followed by a more detailed account of the toxic properties of a few representative insecticides. Much of this information has been obtained from animal experiment.

1. General Nature of the Hazards

In Great Britain the manufacture of the active ingredients of most of the insecticide preparations on the market is in the hands of one or two firms. These firms are well aware of the poisonous nature of the materials they handle and, because they have an extensive experience of the manufacture of poisonous compounds, they are able to take full and adequate protective measures. While the potential hazards are probably greatest at this stage, the population exposed to risk is small and well protected.

These active ingredients are next distributed to a large number of firms, varying considerably both in size and in standards of efficiency. They manufacture a great variety of preparations of the active ingredients in the form of dusts, smokes, liquid concentrates, aerosol spray mixtures, etc. Such manufacturers may not always be aware of the special difficulties of controlling dusts, and reports from abroad have shown that fatalities may occur when the more toxic of these insecticides are made up into powders. The manufacture of such powders should be actively discouraged. Many of these firms also have experimental gardens, orchards, hothouses, etc., where their preparations are first tested before they are marketed. As a general rule no new preparation will find a ready market in Great Britain until it bears the official approval of the Ministry of Agriculture. This approval means that the material will be effective for the purpose described on the label and if used in the manner recommended by the manufacturer. The Ministry also sees that the material is labelled correctly in accordance with the regulations contained in the Pharmacy and Poisons Act, 1933.

The employees of the firms making these preparations form a group of considerable size and one which is particularly

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TOXIC INDUSTRIAL SOLVENTS

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exposed to severe toxic hazards. The manufacturing facilities and safety measures may be deficient. The workers in the field may be handling the materials for many hours each day and for periods extending over several weeks. They may be using new compounds about which very little is yet known. These firms, as a rule, belong to the Association of British Insecticide Manufacturers. This Association collects and distributes all available information on the toxicity of insecticides. Although the population at risk is somewhat larger than in the group manufacturing the active ingredients, it works on the whole under careful supervision and the employees are kept well informed about the properties of the materials they handle.

The application of the insecticides to crops provides the next point of danger. A large number of people, including not only farmers, market gardeners, and their employees, but also the ordinary private citizen, are able to purchase these insecticidal preparations. They may have no more knowledge of the properties of these insecticides than is contained on the label or leaflet supplied by the manufacturer. In some cases the materials may be given to unskilled workers, with only oral instructions as to their use and method of application. It will not be possible to see that proper precautions are observed, and in many cases the men will be far from washing facilities, and will have no opportunity to change their clothing in the event of accidental contamination. Also there will always be the individual who thinks that he can increase the efficiency of a preparation by using it at a concentration several times greater than that recommended by the manufacturer. At the present time the manufacturers of the new organo-phosphorus insecticides have agreed not to make them available to the retail trade.

Within this population there is one group that is exposed to special risks, namely, the employees of firms which undertake contract spraying. Where the farmer or gardener treats his own crops, the work of applying insecticides will be only one among a variety of tasks. The employees of a contract spraying firm may have this job as their sole occupation for periods of many weeks. They may handle large amounts of concentrated mixtures which they have to feed into their machines. The latter require cleaning and possibly repairs. The men may work long hours during fine weather in the summer months, and they may be far from home and living under relatively primitive hygienic conditions. Though the foreman may be intelligent, the ordinary operative may not necessarily be so, and proper supervision may be impossible under the conditions in which the work has to be done. It is perhaps significant that deaths among men handling agricultural chemicals in this country have within recent years been almost entirely confined to the employees of such firms.

While the dangers to those making and applying insecticides are appreciable, they can to a large extent be assessed. Precautionary measures can be recommended and, in general, enforced. While failure to take the proper precautions may have serious consequences, the onus of seeing that the precautions are observed rests to a large extent upon the potential victim himself. In addition, the fact that there has been access or exposure to a poisonous insecticide would usually be appreciated by a medical practitioner called in to treat illness among this particular section of the population.

A much more insidious danger, about which little or nothing is yet known, may be associated with the marketing of foodstuffs contaminated by insecticides. The whole population, young and old, sick or healthy, are involved and exposed to risks about which they may know absolutely nothing. It is not so much the acute or subacute effects following exposure for short periods that must be considered, but the ingestion of small quantities over periods of years. There is no central authority with power to control the exact ingredients of the nation's foodstuffs, but even if such a body did exist it might have considerable difficulty in acquiring the information it needed to make recommendations for limiting the concentration of insecticides in different foodstuffs. It is often a relatively simple matter to deduce from animal experiment the dose of a new poisonous material that would produce acute or subacute symptoms of poisoning in man. But the effect of feeding small quantities of a toxic material over the greater part of the life span of experimental animals may be impossible to assess even in the animal population itself.

Sometimes there is a tendency to belittle the risks associated with the contamination of food by insecticides. It is true the risk may not seem great if a single item of the dietary is considered alone. But nowadays it is not justifiable to do this. Many items among a variety of foods may be contaminated to a small extent by a number of different insecticides. Fresh fruit and vegetables may be sprayed before harvesting; cereal crops and forage may be treated during storage and then fed to both man and his domestic animals. The latter may store the substances in their tissues or excrete it in milk or eggs. The cumulative effect of some of the new insecticides and the power of the body to store others lend added urgency to the need for acquiring more information on chronic poisoning by insecticides, before their use becomes too widespread and accepted as a part of normal agricultural practice. Already there have appeared instances where vague illnesses have been ascribed to the ingestion of DDT by members of the general population (Biskind, 1949). It is difficult entirely to discount such reports in the absence of more information on the chronic toxicity of DDT.

2. Toxic Properties of Certain Typical Insecticides

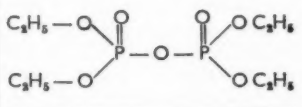
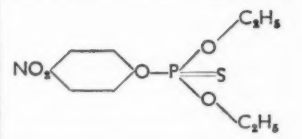
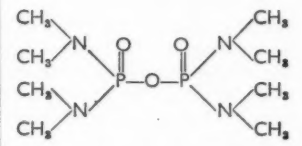
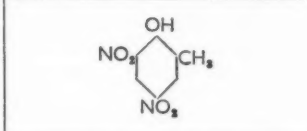
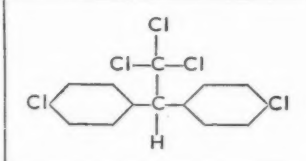
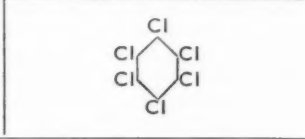
In discussing the poisonous properties of insecticides reference will be made to only a few representative examples (see Table 1).

Certain insecticides of natural origin have been in use for many years. Pyrethrum and derris have never been responsible for poisoning in man, although pyrethrum is liable to cause a sensitizing dermatitis among workers processing the dried flowers. Little is known about the mode of action of these compounds in insects or in mammals.

Nicotine is another natural insecticide that has been in use for many years and it can be said with some truth that few of the modern synthetic insecticides are any more poisonous than this compound. During the period 1931–47 there were 13 deaths from accidental nicotine poisoning in England and Wales. Unfortunately, it is not possible to say how many of these deaths occurred among those handling insecticide preparations of nicotine.[1] Nicotine is a poison with a very rapid action and is readily absorbed by mouth, by inhalation, and through the intact skin. However, the early symptoms of nicotine poisoning are familar to most adults and it is possible that this early recognition may have enabled suitable prophylactic and cleansing measures to be carried out promptly.

[1] I am indebted to Dr Percy Stocks of the Registrar General's Office for the figures of deaths from nicotine poisoning.

TABLE I. SOME TYPICAL INSECTICIDES

Insecticide	Chemical structure
Tetraethyl pyrophosphate (TEPP)	
o-o-p-Nitrophenyl-diethyl-thiophosphate (Parathion)	
Pyrophosphoric tetrakis dimethylamide (PTDM)	
3:5 Dinitro-orthocresol (DNOC)	
Dichlorophenyl-trichlor-ethane (DDT)	
Benzene hexachloride (gamma isomer) (BHC)	

a. Tetraethyl Pyrophosphate and Parathion

TEPP and parathion have both been recommended to be used as substitutes for nicotine. They resemble nicotine in the ease with which they are absorbed by all the ordinary routes, including the intact skin. TEPP is an extremely poisonous compound; the injection of 0.1–0.2 mg./kg. body-weight has proved fatal. The effects on man of a single lethal dose are not known but symptoms would probably include tightness of the chest, salivation, lachrymation, nausea, vomiting and colic with muscular fasciculation, and weakness. The respiratory symptoms would be more pronounced after inhalation and local fasciculations might first appear beneath the site of absorption through the skin. This certainly happens in experimental animals. In these, too, when death occurs after a single dose it always does so within half an hour. If the animal survives for this period then it gradually recovers, with residual muscular weakness and fasciculation persisting for 24–48 hours. The animals remain susceptible to much smaller doses for several days.

The single lethal dose of parathion when injected subcutaneously is at least 100 times as great as that of TEPP and death may not take place till 1–3 days later; the symptoms of poisoning do not appear for several hours if pure preparations are injected. Death in both cases seems to be due primarily to failure of the muscles of respiration.

Both TEPP and parathion irreversibly inhibit cholinesterase and the mechanism of their action has recently been studied in detail (Aldridge, 1950). TEPP is much the more powerful inhibitor but in dilute solutions it is very unstable and is rapidly hydrolyzed to innocuous ethyl phosphates. Parathion, on the other hand, hydrolyzes slowly even in dilute solutions. It is tempting to believe that the delayed deaths which follow a single subcutaneous injection of parathion are due to slow absorption from the site of injection, leading to the gradual inhibition of all the body's available cholinesterase. The rate of inhibition is assumed in these cases to be greater than the rate at which the body can replace the enzyme. However, even more striking delays in the time of death can be seen after the injection of certain analogues of parathion, e.g. with (i) *iso*propoxy groups in place of the ethoxy, and (ii) 8 : hydroxy quinoline in place of the *p*-nitrophenol. Several days after a single injection of a larger dose—250–1,000 mg./kg. body-weight—symptoms first appear and death occurs from 10 to 14 days later, with all the characteristic symptoms of poisoning by cholinergic drugs. It is difficult to believe that these substances injected in very small amounts can remain in the tissues unchanged for days. Any other similar compound would be broken down or excreted long before this. The evidence suggests that the compounds do become selectively fixed somewhere in the body and exert their toxic effects only as they become hydrolyzed.

These observations on animals indicate that parathion may act as a very insidious poison. Reports received recently from abroad show that, with a single exception, death from parathion poisoning has taken place 12–36 hours after the probable exposure to the compound and that progress towards death is relatively slow. The initial symptoms of poisoning have been vague and not characteristic of anything but general fatigue—headache, dizziness, etc. Later, symptoms characteristic of poisoning by cholinergic drugs have appeared.

Laboratory experiments have shown that the symptoms of acute poisoning by TEPP or parathion may be relieved by large doses of atropine. But the real cause of death in acute cases is paralysis of the respiratory muscles. If artificial respiration is given, an animal may survive an otherwise fatal dose, for the diaphragm will recover after a relatively short period of rest—2–5 minutes in the case of TEPP poisoning. In a single published case artificial respiration carried on for two hours saved the life of a man poisoned by parathion (Andersen & Jersild, 1948).

Subacute poisoning by TEPP and parathion is probably a much more serious danger. Fortunately a certain amount is known about the effects of TEPP because it has been used to treat patients suffering from myasthenia gravis. If repeated sublethal doses are given once or twice a day, symptoms of poisoning may eventually appear. This is not because of the accumulation of TEPP, which is rapidly destroyed in the body, but because the regeneration of cholinesterase is a relatively

slow process. Symptoms of poisoning will appear if enough TEPP is given to destroy more enzyme than the body can replace in the time between the doses of TEPP (Harvey, 1948). In myasthenic patients the symptoms of poisoning take the form mainly of abdominal pain, colic and diarrhoea. Because of its stability and slower rate of action it might be expected that parathion would be even more liable to produce subacute poisoning but so far no characteristic cases have been described.

A useful guide to the health of workers handling these compounds might be the determination of their blood cholinesterase levels. Unfortunately, there is nothing yet published about the value of such tests beyond a statement that symptoms do not appear until the level has been depressed to at least 30 per cent of normal (Conley, 1949).

Because of the instability of TEPP the dangers of poisoning with this insecticide are likely to be confined to those who make or apply it. Only very dilute solutions are recommended and these will hydrolyze completely in a few hours. Its effect on insects is correspondingly short-lived. Parathion may prove more popular because its effects last longer and it remains active for many days. This naturally increases the danger to those who collect or consume recently treated crops.

Little is yet known about the effects of ingesting small quantities of parathion over long periods. Experiments that have been in progress for 6 months with rats suggest that there is a relatively sharp line dividing the obviously toxic from the apparently harmless level in the diet. Above a level of 50 p.p.m. in the diet, rats show symptoms within 1–2 weeks and these gradually get worse until the animals begin to die. Below this level no symptoms have been seen and at 10 p.p.m. the rats have reared normal, apparently healthy, families. At the 50 p.p.m. level one group had a 40 per cent death rate within 6 weeks, while in a second group at the same level only a few animals showed symptoms. If the survivors of groups in which 80–90 per cent have died are put back on a normal diet they rapidly recover and gain weight. These survivors, too, have reared normal families after their return to a normal diet.

Denz (in press) has made a careful study of rats poisoned both acutely and chronically with parathion. His examination of the tissues included the central nervous system, and the myoneural junctions. There was no evidence of any permanent structural damage to important organs. Changes are seen in the salivary glands and exocrine parts of the pancreas, but these changes are the same as those described by several workers in the past who have given animals repeated injections of acetylcholine. The tissue reactions are quite characteristic and easy to recognize but cannot in any way be considered adequate to explain the death of the animals.

These observations are encouraging in that they hold out the hope that non-fatal poisoning in man will have no unpleasant sequelae. However, such experiments do not help in assessing the possible *symptoms* of poisoning. These drugs will have effects upon the activity of the smooth muscle of the intestinal tract and bronchial tree.

b. Pyrophosphoric Tetrakis Dimethylamide

PTDM is one of a group of systemic insecticides[1]. These compounds have little direct toxic action on insects but if they are watered on to the soil or the leaves of a growing plant they are taken up by the plant, and insects feeding on the plant are killed (Ripper, Greenslade & Lickerish, 1949). Such compounds are likely to become very popular, because they have a selective effect and kill only the insects that are actually damaging the plant. Insects that kill crop pests are not destroyed, as they may be by the contact insecticides.

If PTDM is added to cholinesterase in vitro it has no inhibitory effect even in a concentration of 1 per cent. When a single dose of 20 mg./kg. body-weight is injected subcutaneously into an animal, symptoms of poisoning by a cholinergic drug appear in about 15 minutes; the animal dies within 30 minutes and the level of serum- and red blood-cell-cholinesterase is found to have fallen to zero. In other words, the body has converted PTDM into an anticholinesterase drug. It is possible that plants also make such a conversion, or that the conversion takes place in the tissues of the insect after it has fed on the plant juices containing PTDM. The absence of any direct effect of PTDM on insects suggests that the plant brings about the conversion. Plants receiving a single treatment may remain poisonous to insects for several weeks, suggesting that PTDM is very stable, and that an extremely active insecticide is produced by the plant.

The effects of the ingestion of small quantities of PTDM over long periods urgently require investigation. Although the toxicity of PTDM itself is apparently of the same order as that of parathion, nothing is yet known about the properties of the active ingredient produced by the plant. Plants treated with such an insecticide obviously cannot be freed from it by any cleaning process. It should be emphasized that there is no direct evidence that the plant does convert the PTDM to the actual compound.

c. 3 : 5 Dinitro-Orthocresol

DNOC is another substance that acts characteristically as an acute poison, though its actions are in no way related to those insecticides discussed above. Animal experiments show that it does not act as a cumulative poison, nor do animals become significantly resistant to increasing doses. A single dose produces an acute metabolic disturbance, characterized by dyspnoea, pyrexia and muscular weakness. Death ensues within a few hours or else the animal recovers completely within 24 hours. No structural changes are produced in vital organs by repeated injections of toxic but sublethal doses. In vitro observations have shown that solutions of DNOC, in common with related dinitro compounds, uncouple phosphorylation from oxidation, so that the former process is inhibited while the latter proceeds at a greatly increased rate.

DNOC has been widely used in Britain as a winter wash for fruit trees and no cases of poisoning have been recorded, although the operatives may become very obviously contaminated by the solution when large-scale apparatus is being used. DNOC is also used as a selective herbicide and it is among the operatives who apply DNOC for this purpose that deaths have occurred in recent years. The symptoms of poisoning are similar to those seen in animals, and death is characteristically sudden. This difference in incidence and in results between these two groups of operatives is interesting. The probable explanation is that for weed killing DNOC is used in solutions 10 times as strong as those used for winter

[1] More recently this insecticide has been called octa methyl pyrophosphoramide (OMPA).

washes. Weed killing operations are carried out in May and June when the days are long and the weather may be hot, so that the workers are wearing only a few thin clothes. These conditions are the antithesis of those which characterize winter-wash operations. DNOC is never applied under conditions where food crops would become contaminated.

d. Dichlorophenyl-Trichlorethane and Benzene Hexachloride

DDT and BHC can be considered together because they have many properties in common. As they are both stable compounds and persist on materials that have been treated with them, their toxic properties are of special importance. Both are virtually insoluble in water, and their acute toxicity is low. A few cases of acute poisoning by DDT have been reported. Usually they resulted from the accidental incorporation of large amounts of DDT in prepared food. A number of other cases of acute poisoning with solutions of DDT have been described but the poisonous effects recorded were those of the solvent rather than of the DDT itself.

Little is known about the mode of action of DDT and BHC. The symptoms of intoxication, with widespread tremors developing into clonic convulsions, indicate some disturbance of the nervous system. Dresden (1949) has suggested that DDT affects nerve ganglia so that a single afferent impulse in a reflex arc will result in multiple efferent discharges. The behaviour of the central nervous system and the myoneural junctions remains unaffected until death. The gamma isomer of BHC is a convulsant. The beta and delta isomers are depressants and counteract the effect of the gamma isomer.

These compounds are used widely for a great variety of purposes. Growing crops and stored grain, domestic animals and their quarters, and public eating places may all be treated with solutions or powders containing DDT and BHC. Thus fresh food, manufactured food, meat, milk, eggs or eating utensils may all carry traces of the compounds. DDT is tasteless and odourless, so that its presence will not be detected by those consuming it. The older preparations of BHC imparted a characteristic taint to food. Though newer preparations do not do this, it is questionable whether the public would not be better served if only strongly tasting or highly odorous insecticide preparations were used!

Several long-term feeding experiments have been carried out with DDT and some emphasis has been placed by American workers on the liver lesions produced by DDT (see Glassman & Buchan, 1948); Dunbar (personal communication, 1949) has recently reported liver lesions in rats receiving as little as 5 p.p.m. DDT in their diet. The significance of these histological changes is open to question. Cameron & Cheng (personal communication, 1949) have recently examined the tissues of rats that had received DDT daily for up to two years in amounts of 35 and 350 p.p.m. They found that the changes in the livers of these animals, with two exceptions, were not significantly different from the changes in control rats.

This example of differences of opinion serves to illustrate the extreme difficulty of trying to evaluate the results of long-term feeding experiments in animals in the absence of any striking change that would immediately condemn the material as poisonous.

3. Conclusions

There seems little likelihood that the difficulty of interpreting the chronic effects on experimental animals will ever be solved. The effect of small doses of some compounds might be detected if something were known about their precise mode of action. Suitably sensitive biochemical tests might be devised on the basis of more knowledge of the action of the poison.

Those having the responsibilities of safeguarding the public health are faced with two possibilities: either the use of the compounds may be prohibited altogether and agriculture and animal husbandry thus be robbed of several most important aids; or the public may be allowed to consume very small quantities of materials which, given in equivalent doses to experimental animals, appear to be completely harmless.

The ideal solution would be to see that all food consumed by the public was free from any insecticide that might have been employed at any stage in its growth or manufacture. It is essential that suitable micromethods for determining these compounds should be devised. Those interested in the manufacture and use of these compounds should be encouraged to devote more effort to the study of methods of analysis and the mode of action of the materials they produce. Instead, more and more new compounds are now being produced, about whose toxic properties less and less is known.

It may be that the insecticide that is ideal from the agricultural point of view is one that is highly dangerous to public health. At the present time there is little interference with the use of new insecticides. If any evidence appears that the health of the consumer may be menaced by the use of these compounds, suitable legislation might have to be introduced. Those interested in the use of insecticides would do well to pay more heed to the possible risks to public health that might attend the use of the particular materials they favour. It may be much cheaper to treat crops with a single application of a stable persistent material of a relatively low acute toxicity so that it can be safely handled by unprotected or unskilled workers. On the other hand, considerations of public safety might eventually make it necessary to limit insecticides for use on foodstuffs to those that are highly active but are unstable and readily decompose into innocuous breakdown-products.

The assessment of the toxicity to man of any particular compound that is not obviously very poisonous to animals is a difficult, time-consuming and expensive task. There is, therefore, great need for active co-operation between entomologists, plant pathologists, and those working on mammalian toxicology, so that full investigations are carried out only on materials of proven value as insecticides.

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OCCUPATIONAL SKIN DISEASE

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1 Studies of national statistics
  a Studies based on reports from examining surgeons
  b Studies based on voluntary notifications (Birmingham area)
2 Clinical studies in factories
  a Skin disease in an engineering factory
3 Laboratory investigations
  a Bacteriology
  b Other pathological investigations
4 Prevention and treatment
References

Industrial dermatitis has been recognized for many years as the main cause of lost time among the prescribed diseases for which workmen are entitled to compensation. We have found that in recent years the apparent incidence of dermatitis has risen markedly. The team set up in the Birmingham Accident Hospital by the Medical Research Council to study industrial medicine has therefore made the investigation of skin diseases in factories an important part of its research programme. The following review embodies the major results of this work as well as some reference to other publications on the subject.

The problem of this group of disorders is not a simple one, and can be investigated comprehensively only along general biological lines. Our object has been to collect concrete facts likely to be useful in reducing general disability, and it is already clear that certain recommendations, if followed up, can lead to appreciable economic saving to the nation, to industry and to the workpeople. The general plan of investigation has fallen into three main sections:

i. A critical examination of statistics derived from returns available on a nation-wide basis, giving incidence, trends, and broad differences between industries;
ii. Clinical investigations of patients in local factories, showing the detailed relations between the sick man and his job;
iii. Laboratory investigations of particular features of the disease (e.g., bacteriology of normal and diseased skin), of some properties of normal skin (e.g., biochemistry of surface lipids), of specific hazards, and of possible preventive or curative measures.

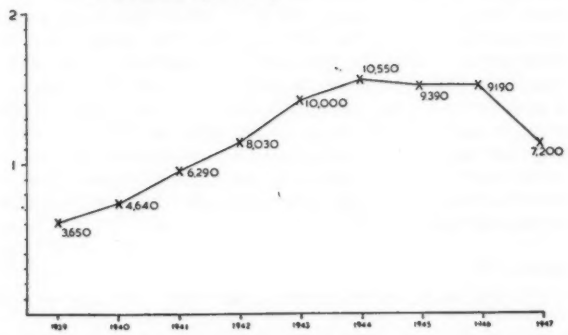
1. Studies of National Statistics

Two series of statistics are available for the over-all study of industrial dermatitis. They are derived independently from the certificates given by examining surgeons (appointed factory doctors) to workmen seeking compensation for industrial dermatitis and from voluntary notifications made by various firms to medical inspectors of factories. These notifications, although of very great value to the factory inspector in providing information about local conditions, and leading to the giving of constant help and advice by the Factory Department of the Ministry of Labour, are, like all forms of voluntary notification, incomplete. This was well shown by Henry (1943) for the pre-war period when comparison was made between the number of cases voluntarily notified and the figures based on examining surgeons' reports. These reports are also liable to inaccuracies, though of a much smaller order. For instance, in some large firms the factory medical officer also advises the firm's insurance company which, up to July 1948, had usually been responsible for paying compensation. Under these conditions, a man may properly be awarded compensation without necessarily reporting to the examining surgeon. Again, during the war years some factory employees, under the Ministry of Supply for instance, were compensated under separate schemes, and have not therefore been reported. For these reasons, the figures now to be discussed may be somewhat low. On the other hand, a certain number of the cases considered eligible for compensation by the examining surgeons are subsequently rejected by medical referees when the claim has been disputed; precise records of these numbers were not readily available to us. These disturbing factors are, however, considered to be small, and not likely to interfere with the general picture.

a. Studies Based on Reports from Examining Surgeons

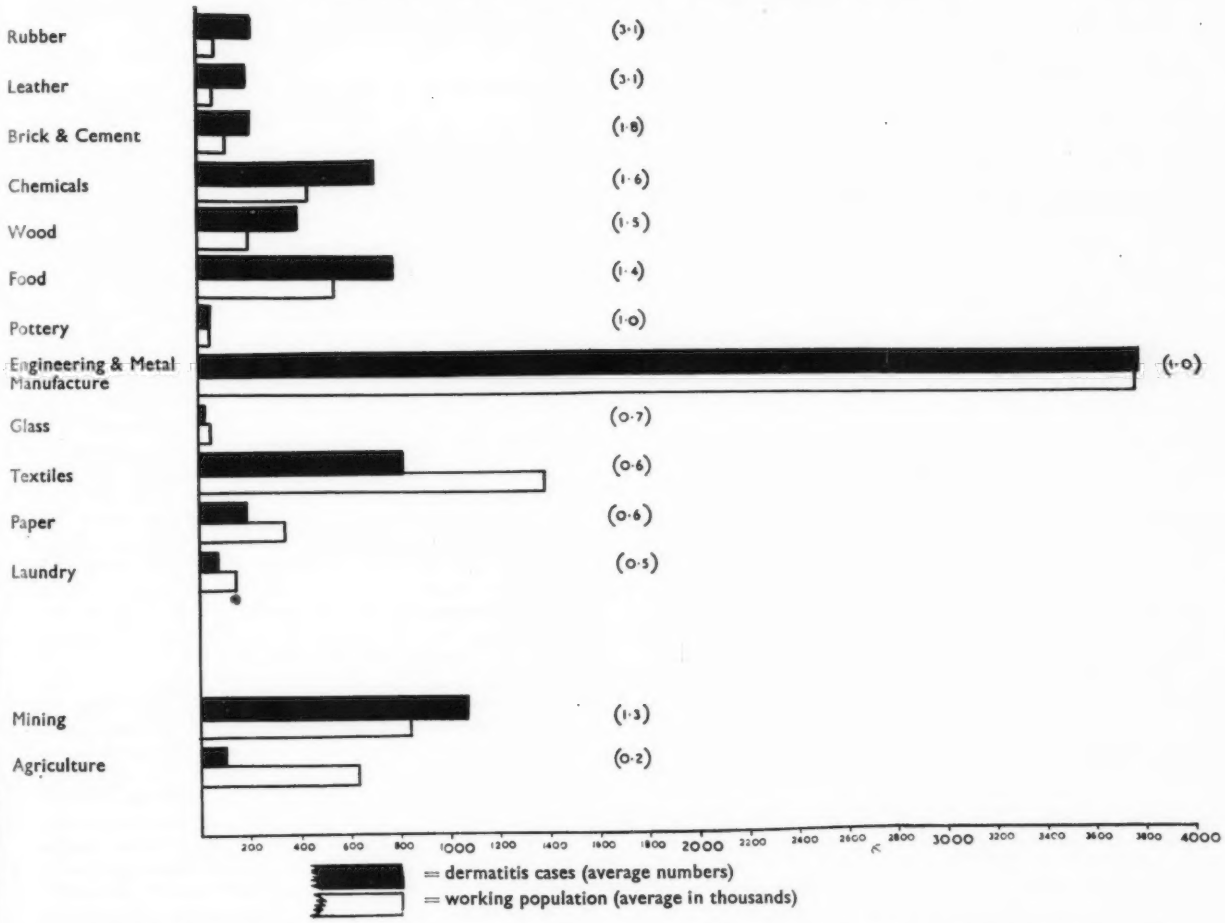
Figure 1 shows approximate numbers of cases of industrial dermatitis, calculated from the examining surgeons' reports, which have occurred in factories year by year from 1939 to 1947. It will be seen that the annual total of these cases, which numbered some 3,600 in 1939, rose to over 10,500 in 1944, and has subsequently tended to fall slightly. The figure for 1947 must be regarded as atypical, being considerably influenced by the closing of many factories in the spring because of the fuel crisis. All these figures, of course,

FIG. 1. APPROXIMATE INCIDENCE OF INDUSTRIAL DERMATITIS IN ALL MANUFACTURING INDUSTRIES (1939–47)



Ordinates: Incidence per 1,000 employed. The cases included were those reported to examining surgeons as losing three or more days of working time. The graph shows incidence based on these numbers and on appropriate factory populations

FIG. 2. AVERAGE NUMBERS OF DERMATITIS CASES COMPENSATED ANNUALLY COMPARED WITH AVERAGE WORKING POPULATION IN VARIOUS INDUSTRIES (1939–46)



Numbers in brackets represent average incidence in cases/thousand employed/year, i.e. cases ÷ working population (in thousands)

refer to cases sufficiently severe to cause more than three days' absence from work, and which have been considered by examining surgeons as being occupational in origin.

Crude figures of the occurrence of disease may often be misleading unless considered in relation to the size of the population from which they are drawn. Approximate figures were therefore obtained for the population (given in thousands) working in factories in each year. These figures were taken from the statistical reports issued by the Ministry of Labour, and are conveniently available in the *Annual abstract of statistics* published by His Majesty's Stationery Office, London. When the figures for the occurrence of dermatitis are divided by these populations to give an incidence of dermatitis cases occurring each year per 1,000 factory workers, confirmation is obtained of the considerable rise in incidence; i.e. from about 0.6/1000/year in 1939 to over 1.5/1000/year in the years 1944–46. The annual incidence calculated in this way is plotted graphically in fig. 1.

National figures can be used to give reasonably precise indications, not only of the magnitude of the over-all problem, but of the main sections of industry in which it lies. The average numbers of dermatitis cases in various industries compensated annually for the years 1939–46 are shown in fig. 2 (black blocks); alongside each of these is shown a clear block, giving the numbers in thousands of those employed in each industry. The incidence of dermatitis in an industry is, of course, given by the ratio of the black block to the clear block and is shown in brackets alongside each industry. These figures were necessarily subject to minor errors dependent on each patient's version of the industry in which he was employed, but they appear sufficiently accurate for general purposes. It may be concluded, for instance, that while the range of incidence is fairly wide between different industries, e.g., about 3/1000/year for the rubber and leather industries, against 0.5–0.6/1000/year for such industries as textiles, paper, laundry, etc., no industry is exempt, and the

problem is widespread throughout all kinds of factory. The differences clearly require close study within each industry, and if sub-groups are taken, much higher incidences may be found for limited classes of workers. For instance, although the textile and clothing industry as a whole has a fairly low incidence of dermatitis, the processes of bleaching and dyeing textiles appear to have a high incidence, no doubt because of specific exposures and other factors in the work. Again referring to fig. 2, the relative size of the black blocks indicates where the majority of cases are to be found, and it is strikingly evident that the large group of " engineering " factories (in which we have included those engaged in metal manufacture, vehicle, aeroplane and shipping construction, etc.) produces the largest number of cases. About 3,800,000 workers are employed by this group—rather more than half of the number working in factories in this country. Of these, in the period 1939–46 about 3,800 contracted dermatitis each year, i.e., nearly half the total number of cases. Further subdivision did not lead to any useful distinction between different parts of this industrial group.

We may now briefly consider the rise in the incidence of dermatitis (1939–46) shown in fig. 1. It might be thought that this rise was due to the transference of workers from low- to high-risk occupations (e.g., into such factories as those turning out explosives, many of which are known to be potent dermatitis-producing agents). This idea can be discounted by considering the annual incidence for each of the years 1939 to 1946 separately for each industry. In fig. 3, these have been shown as continuous lines, which may be compared with the dotted line showing incidence for the manufacturing industry as a whole, previously given in fig. 1. It can be seen at once that the rise in the incidence of dermatitis has been a general occurrence throughout all the industries in the country. Attempts to relate the size of this increase to such factors as the increase or decrease in the working population in each industry during the war years have been unsuccessful. The rise has been widespread, and since some of the industries concerned are of a traditional type with no marked change in technology during the war years and no obvious introduction of fresh hazards, the problem appears to depend mainly on a general social change rather than on new chemical or physical hazards. Special difficulties occasionally arise in an industry, as, e.g., in the brick and cement group in 1946 when the labour force was suddenly almost doubled.

It will be shown later that many more factory workers contract dermatitis than seek to go off work. The exact proportion who are willing to lose time, and therefore wages, and to risk possible replacement by other men with no disability, may vary from time to time. It seems to us that the present rise in dermatitis incidence is unlikely to be due to an actual major increase in the disease, and is more likely to be simply a manifestation of the sense of security on the part of the workers and their growing attention to medical disorders. If this interpretation is correct the real problem, even of the magnitude it now assumes, has always been with us. If the present state of full employment were to be lost, it is possible that fewer men might be willing to go off work, but they would still be suffering from skin disease. It is unsound to regard this problem as one temporarily exacerbated by the abnormal conditions of the war and immediate post-war period. The extent of the trouble must be faced, and if it is considered excessive (as surely it must be) new ways must be found both of preventing the occurrence of skin disease and of curing it more rapidly and more completely. Accurate figures are not available for other countries, but there are indications (Schwartz, Tulipan & Peck, 1947) that there are even greater incidences among industries in the USA.

b. Studies Based on Voluntary Notifications (Birmingham Area)

As already explained, the voluntary notifications are numerically incomplete. Most large firms notify all cases going off work ; though, theoretically, they might also notify milder cases, in practice this is rarely done. Some large firms and many small ones do not notify any cases. In the Birmingham area, at present, about half of the cases going off work are notified.

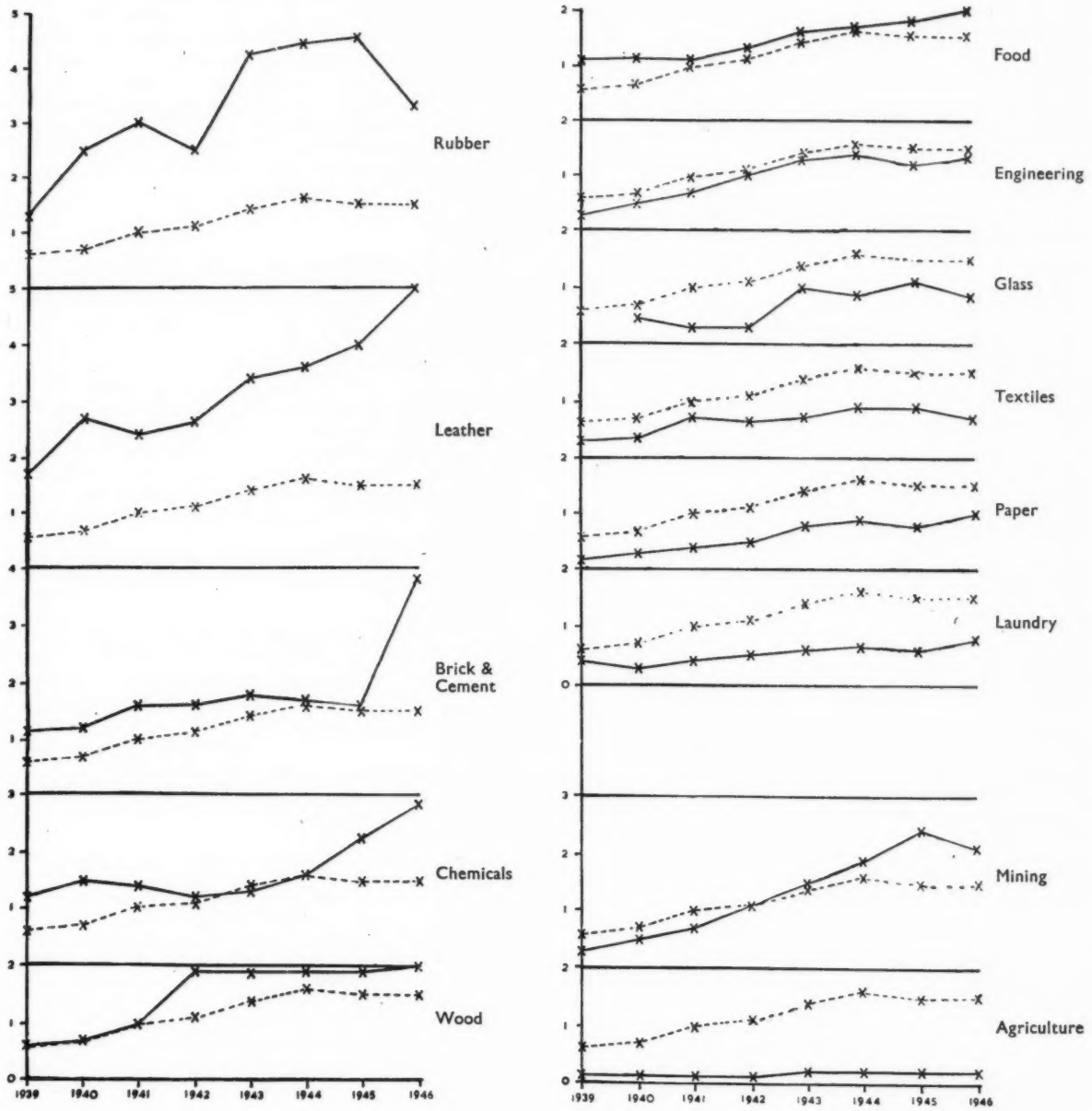
The information given on the voluntary notifications is much more detailed than that supplied by examining surgeons. It includes the nature of a firm's business, a worker's precise occupation, age and sex, the date when he went off sick, together with a column for remarks, in which the part of the body affected and the possible cause of the condition are often listed. We have been enabled to make certain analyses based on the voluntary notifications in the Birmingham area. By listing the occupations of all cases notified during the years 1946 and 1947, it was apparent once more that nearly half the cases occurred among metal workers. If those engaged in plating were included, it was evident that the majority of cases were occurring in the engineering industry. The numbers of workers in various jobs will not be available on a regional basis until the results of the next census are known, so that the incidence of dermatitis in different occupations cannot be determined exactly. But approximate calculations show that certain groups have abnormal risks. Like the national statistics, regional figures indicate the existence of high-risk occupations but most cases occur in common occupations without obvious major hazards.

Analyses have also been made of the sex and age incidence of dermatitis cases. Roughly twice as many men are affected as women, but this corresponds with the ratio of the numbers employed. Age classification shows that all ages are affected ; about 5% of the males reported are over the age of 65. If the males are divided into five-year groupings, over the age of 30, the relative numbers affected correspond very closely with the distribution of these different groups in the general population. Under the age of 30, the figures are probably still affected by the numbers of men liable to military service, and precise figures for different ages within industry are not at present available. Among females, there is a notably low occurrence during the child-bearing years, presumably because women of this age are not so widely employed. Also, fewer women are affected over the age of 50, probably because of the earlier retirement of women from industry.

Analysis has been made of the numbers notified in each month for the years 1945–47. There appeared to be little seasonal effect on the occurrence of dermatitis, though the effect of the fuel crisis in lowering the incidence in the spring of 1947 was evident.

The analysis of the voluntary notifications according to the part of the body affected yielded information which, taken in conjunction with our individual studies in factories, seems to us to be important. In about 90% of all cases voluntarily notified and mentioning which part of the body was affected, the skin disease occurred on the hands or forearms.

FIG. 3. YEARLY INCIDENCES OF DERMATITIS IN VARIOUS MANUFACTURING INDUSTRIES COMPARED WITH OVER-ALL AVERAGES FOR MANUFACTURING INDUSTRY AS A WHOLE, IN THE UNITED KINGDOM (1939–46)



Of the remainder, two-thirds were affected on the other exposed parts, i.e., the face and neck. The causative agent regarded as responsible was most frequently oil or " suds ", that is, an emulsion of oil or other substances in water, used for cooling the cutting edges of tools in mechanical lathes, etc. The exact significance of these causative agents cannot, however, be assessed from notification papers, since the wording of the compensation regulations (" dermatitis due to dust or liquids ") leads rather naturally to mention of the liquids most commonly encountered in the course of a man's work. Of general importance also is the frequency with which minor abrasions or burns are mentioned, both of them being commonly spoken of as having led to sepsis. Reactions to dressings are occasionally described. The voluntary notifications for the Birmingham area form a natural bridge between the national statistics based on the examining surgeons' reports and our detailed studies in local factories.

2. Clinical Studies in Factories

As indicated in figs. 2 and 3, certain industrial groups suffer a high incidence of dermatitis. Individual factories within these groups may show even more strikingly the effects of working with irritating or sensitizing chemicals. In a leather factory with a pay-roll of 160 workers, medical inspection of all the workers showed 16% with dermatitis. The incidence was highest (28%) in the dyeing section where notorious sensitizers such as formaldehyde, lacquer and Bismarck brown were used. In a felt hat factory three of the five workers employed on dipping felt " cones " in sulphuric acid had dermatitis, while the over-all incidence of occupational skin disease in the factory was 6% (excluding those workers who suffered only from the occupational stigmata associated with the process of forming the hats). In a small shop of a factory where pyrethrum powder was handled in the process of preparing insecticides, only eight men were engaged at any one time during a period of seven years; yet during this period 28 men had contracted dermatitis necessitating absence from work and had nearly always to change their jobs (see also Martin & Hester, 1941). Such an instance is striking, and the elucidation of the exact nature of the sensitizing and irritant substances is full of interest. Much of the literature concerned with industrial dermatitis is devoted to such problems. They are not, however, representative of the less dramatic but much more widespread difficulties in the typical industrial groups of this country which we have classified together as " engineering ".

a. Skin Disease in an Engineering Factory

A typical light engineering factory was selected for intensive study. It was specially suitable for a number of reasons: (i) the pay-roll included over 5,000 manual workers and nearly half as many non-manual workers (office staff, factory clerks, supervisors, etc.) who served as a control group; (ii) the general nature of the work of the firm was engineering (the trade providing most cases of dermatitis) but it included a wide variety of processes—metal work with automatic and semi-automatic lathes, welding, casting, hardening, painting and enamelling, electroplating with chrome and nickel, degreasing and light assembly; (iii) the firm was compactly arranged round a central medical department which included a popular medical officer and very efficient records and nursing services.

All patients with skin disease (other than simple boils or scabies) of sufficient severity to need medical attention were asked to attend a weekly clinic which was run by the research team in conjunction with the factory medical officer. Both manual and non-manual workers attended this clinic, irrespective of whether the condition was presumed industrial or not. A careful history was taken on first attendance, and often amplified later. After physical examination and further investigations (bacteriology of lesion, nose and normal skin, urine testing, blood examination when required, etc.) treatment was prescribed and usually given in the factory surgery. Photographic records of progress were made in a large proportion of patients, and have been very valuable.

i. Incidence

During the two and half years under consideration (1946–48), 123 patients reported to the clinic with an attack which had commenced within the previous three months; 100 were manual workers and 23 were non-manual workers. Since the average populations were known it is possible to give an over-all incidence of fresh attacks of skin disease among the two groups, viz., 7.8/1,000/year among manual workers and 4.0/1,000/year among non-manual workers. The greater incidence (3.8 cases/1,000/year) among the manual workers can be attributed to the industrial environment if we can be sure that the two groups were equally willing to seek advice from the factory medical department. Evidence that similar proportions did attend is provided by comparing the cases by other objective criteria.

Table I shows an analysis of skin disease in the two groups, further classified according to the part of the body affected.

TABLE I. INCIDENCE OF SKIN DISEASE IN ENGINEERING FACTORY, 1946–48

	Manual workers (population 5,100)		Non-manual workers (population 2,325)	
Part of body affected	Total number affected	Incidence/ 1000/year	Total number affected	Incidence/ 1000/year
Hands or forearms only	41	3.2	4	0.7
Hands or forearms and other sites	28	2.2	4	0.7
Other sites (hands and forearms not affected)	31	2.4	15	2.6
Total	100	7.8	23	4.0

Inspection of the incidence figures shows that disease of parts other than hands and forearms was similar in manual and non-manual workers, while the additional disease in the manual workers, amounting to about 4/1,000/year, was due entirely to an increase in those diseases affecting the hands and forearms. Less objective but nevertheless confirmatory evidence was obtained by listing the skin diseases not affecting hands and forearms according to diagnosis. It will be seen from Table II that the nature and incidence of the various conditions in this group of skin affections are similar in the manual and control groups.

TABLE II. COMPARISON OF SYNDROMES AFFECTING PARTS OTHER THAN HANDS AND FOREARMS OF WORKERS IN ENGINEERING FACTORY, 1946–48

	Manual workers (population 5,100)		Non-manual workers (population 2,325)	
	Total number affected	Incidence/ 1000/year	Total number affected	Incidence/ 1000/year
Lesions of feet (fungal and bacterial infection, etc.)	11	0.9	5	0.9
Acneiform and infective rashes of head and neck	5	0.4	4	0.7
Seborrhoea	4	0.3	2	0.3
Other lesions	11	0.9	4	0.7
Total	31	2.5	15	2.6

As it appears likely that similar proportions of the manual and staff groups did report their skin conditions, consequently it is justifiable to regard the additional incidence of skin disease of the hands and forearms amongst the manual workers as occurring as a result of manual employment. Certainly other differences (social status, earnings, home conditions) exist between the manual and non-manual workers. But if these differences were markedly affecting the liability to skin disease among the manual workers, a difference would surely have been found for skin disease of all parts of the body. The hands and forearms are exposed to added risk of all kinds of trauma among the manual workers, and this is reflected in the high incidence of skin disease of these parts.

This objective demonstration of the amount of industrial skin disease in a factory has been set out in detail, since various conclusions follow. Four cases per 1,000 per year for this typical engineering factory can be given as a figure of the minimum amount of industrial skin disease sufficiently severe to lead workers to seek medical advice; other cases of comparable severity undoubtedly existed, but did not seek attention. This figure is about three times as great as the number who had to stop work and receive full compensation in this factory, and about three times the number recorded as losing work in the national statistics already quoted for the corresponding years.

Again, four out of every five cases of skin disease of the hands or forearms (whether other parts of the body were affected or not) can be regarded as industrial in origin, directly or indirectly. This conclusion suggests that the great majority of cases voluntarily notified to the medical inspectors of factories was, in fact, industrial as, it will be remembered, about 90% of these notifications were of skin disease affecting these parts of the body.

ii. Skin disease in relation to employment

Since it has been demonstrated that manual workers suffer from an increased incidence of skin disease affecting the hands and forearms it becomes necessary to ascertain the factors which might account for this—in other words, the patient must be considered in relation to the type of work he is doing. One difficulty is the fact that, in this factory at least, groups of workers were not employed under completely uniform conditions. It was possible, however, to make rough classifications of the types of work done and to relate these to the amount of skin disease occurring in these groups. Figures for the numbers employed in these categories were obtained from the labour department and the incidence of skin disease is expressed as cases/1,000/year (Table III).

It will be seen that, in confirmation of the impressions formed from the voluntary notifications, some workers in an engineering factory can be classified as at "high risk", e.g., electroplaters, hardeners, welders and solderers, painters and sprayers; some are at "low risk", e.g., assemblers, electrical workers, storemen and packers; and there is an "intermediate" group of machine operators and fitters. It is of particular significance, however, that although machine operating does not rank as a "high risk" trade, it contributes by far the greatest number of cases.

It is clear, however, that simple labelling by trade is not a sufficiently accurate method of determining the actual causes of dermatitis except in clearly defined processes. Thus if the duties of machine operators are considered in detail it will be found that some are exposed to skin contamination by insoluble cutting oils, others work in "suds" and some are employed in "dry" processes. The cases were therefore also considered in relation to possible causative agents. This necessarily involved an approach more subjective than heretofore. In the analysis which follows (Table IV) cases were classified under a specific "agent" only when the etiological relationship appeared clear, and were labelled "non-industrial" only when the diagnosis was beyond doubt. In order to give an indication of the severity of the dermatitis the amount of time lost is also considered.

Consideration of the agents listed shows that oil (mainly cutting oil) was responsible for the largest number of cases but for only a small proportion of the time lost. On the other hand, the oil-in-water emulsion known as "suds" (which is also used on a large scale in this factory) was responsible for only seven cases. Nevertheless, four of these had to go off work, losing an aggregate of 235 days. Although the hazards associated with chrome plating are well known, and intensive efforts are made to control them, 270 days were lost by electroplaters. The number of cases from other causes was too small to justify detailed consideration. In 15 of the 69 cases no clear etiological relationship could be established,

TABLE III. INCIDENCE OF SKIN DISEASE AFFECTING HANDS OR FOREARMS CLASSIFIED BY OCCUPATION IN ENGINEERING FACTORY, 1946–48

Occupation	Approximate population	Total number of cases	Incidence/ 1000/year
Electroplaters	35	11	126
Hardeners, solderers, welders	50	4	32
Painters, sprayers (paraffin) ...	50	2	16
Metal polishers	35	1	11
Foremen, charge hands and viewers	180	3	7
Machine operators and fitters	1950	31	6
Cleaners and canteen workers	180	2	4
Boilermen and labourers ...	315	2	3
Assemblers	1040	8	3
Storemen and packers ...	220	1	2
Electrical workers	500	0	0
Carpenters	50	0	0
Miscellaneous	395	4	4
Total	5000	69	5.5

TABLE IV. PRINCIPAL CAUSATIVE AGENTS ENCOUNTERED BY 69 MANUAL WORKERS WITH SKIN DISEASE AFFECTING HANDS OR FOREARMS IN ENGINEERING FACTORY, 1946–48

Agent	Number affected	Number away from work	Total time lost (days)	Mean time lost (days)
Oil	14	2	39	20
Chrome and nickel ...	8	4	270	68
"Suds"	7	4	235	59
Cleansing agents ...	2	2	137	68
Dressing medicaments	3	1	102	102
Paraffin	2	1	42	42
Alkalis	3	1	30	30
Anti-rust compound ...	1	0	0	0
Doubtful or other ...	15	2	39	19
Non-industrial	14	1	21	21
Total	69	18	915	51

but in this group only two went off work, for a total of 39 days. It is interesting to note that the proportion of non-industrial skin disease based on a clinical diagnosis corresponds closely with that predicted from statistical evidence, i.e., about one-fifth of the cases in which the hands and forearms were affected.

The important conclusion to be drawn from this analysis is that by far the greatest amount of time lost could be attributed to substances which are recognized to a varying extent as potentially harmful, and that consequently a closer study of the methods of using these agents might result in a considerable reduction of the problem of dermatitis.

An illustration of the susceptibility of "green labour" to skin disease was given by the fact that more than one-third of the patients whose hands and forearms were affected sustained their skin disease during their first three months on that particular job. (A small proportion of those with skin disease of other parts of the body were affected within this period.) During the period of study, the factory, like most others, had a relatively high labour turnover and consequently the liability to a high dermatitis incidence was increased. A high labour turnover not only brings more new workmen into an occupational hazard but it also increases the difficulties of their training and education in safety precautions.

iii. Clinical syndromes

The different types of skin reaction affecting the hands and forearms of the manual workers attending the factory clinic are listed in Table V. No form of classification has been found completely satisfactory, and closely similar appearances may be associated with different etiological agents. As already stressed, it is of most value to know the part of the body affected when the diagnosis of industrial skin disease is being considered; it appears important also to note whether the hair follicles are primarily affected. More detailed consideration of the nature of the reaction is only occasionally helpful in diagnosis; for prognosis, an important distinction should be drawn between vesicular and non-vesicular lesions, as will be shown later.

Among the non-vesicular rashes, oil folliculitis (Plate III, fig. D) was a clearly defined condition (White, 1934). It is characterized by the occurrence of "plugs" of keratin in the hair follicles, often visible as comedones and leading to the development of acneiform lesions and papules. Infection by pyogenic cocci, although sometimes complicating the condition, was not necessary for its development. In the majority of workers heavily exposed to cutting oils, oil folliculitis is found if inspections are carried out, though relatively few men report for medical attention. Hyperkeratoses (Plate III, fig. E) are also common after exposure for many years, and squamous cell carcinoma may follow (see Cruickshank & Squire, 1950, for examination of these hazards in the engineering industry).

Fine diffuse folliculitis, an acute irritation of the hair follicles each of which was surrounded with erythema, occurred in some patients as a result of exposure to paraffin or suds. These agents (or perhaps substances dissolved in them) appeared to be responsible for acute vesicular reactions in other patients (Plate III, fig. F; see also Whitwell, 1943). Diffuse folliculitis was also seen as a result of prolonged sweating under rubber gloves. Other non-vesicular lesions not primarily affecting hair follicles included simple erythema due to contact with acute irritants, and papular rashes sometimes attributable to chemicals (Plate III, fig. G), such as chrome solutions.

The vesicular eruptions have been considered separately as of special importance. Some were accompanied by acute erythema, and appeared to be extreme examples of exposure to irritant or sensitizing chemical substances. With these may be considered dressing sensitivity reactions (e.g., to sulphonamides). Sensitivity reactions to the detergent cetrimide (Plate IV, fig. H), widely used for cleansing injuries, have been encountered (Cruickshank & Squire, 1949). These reactions have been classified separately as being "industrial" only in

TABLE V. CLASSIFICATION OF CLINICAL SYNDROMES AFFECTING HANDS OR FOREARMS OF 69 MANUAL WORKERS IN ENGINEERING FACTORY, 1946–48

	Hands or forearms only affected	Hands or forearms and other sites affected	Total
Vesicular eruptions :			
Acute inflammation ...	4	nil	4
Dressing sensitivity reactions	1	3	4
Nummular eczema ...	1	1	2
Recurrent vesiculation of fingers	8	8*	16*
Recurrent vesiculation of palms	2	nil	2
Total	16	12	28
Non-vesicular eruptions:			
Oil folliculitis	5	7	12
Fine diffuse folliculitis	4	1	5
Erythematous and papular eruptions not associated with hair follicles	8	6	14
Other lesions of non-industrial origin (syphilis, tinea corporis, etc.)	8	2	10
Total	25	16	41

* Including 4 patients clearly non-industrial

the sense that the injury was sustained and dressed in the factory. Vesiculation associated with acute erythema often healed rapidly when contact with the offending agent ceased, provided that the horny layer of the skin was not too severely disrupted and that added infection did not occur.

Nummular eczema (Plate IV, fig. J) appeared to be a more sustained reaction of the skin, often to events following minor trauma such as cuts and burns. Only two patients of this series were classified in this category.

Recurrent vesicular reactions appeared to be of great importance and presented considerable difficulty in interpretation. In the past such cases have often been regarded as "eczema" and dismissed as non-industrial in origin. In some at least, recurrent friction or exposure to weak irritants appeared to be instrumental in evoking the rash, as judged by its disappearance over long periods when a patient was transferred from the factory shop into an office. Following vesicular reactions, infections with streptococci (Plate IV, fig. K) and other organisms were often seen (see also below). Prolonged disability also sometimes resulted from dryness, and from scaling and cracking of the horny layer, especially in thick regions such as the palms (Plate IV, fig. L).

There was no evidence of gross nutritional defects in any of the patients. But it was considered likely that skin disease in two of them may have been aggravated by a defective diet. One patient was a newly-returned prisoner of war from a Japanese camp and the other was an elderly man living alone under poor circumstances.

Psychological factors (as detected by general clincial methods) did not appear to be of importance in the causation of industrial skin disease. Occasionally, however, in patients with a prolonged attack of dermatitis it was considered that the patient himself was the greatest obstacle to recovery. This, however, was exceptional. Of greater importance was the number of occasions on which the dermatitis occurred as a result of ignorance or stupidity either on the part of the workman affected or of his supervisors. Thus one of our patients, an old labourer without previous experience of chemicals, was put on to rinsing articles in caustic soda in a mechanically operated barrel; he discovered that the operation could most quickly be performed by removing the articles with his bare hands.

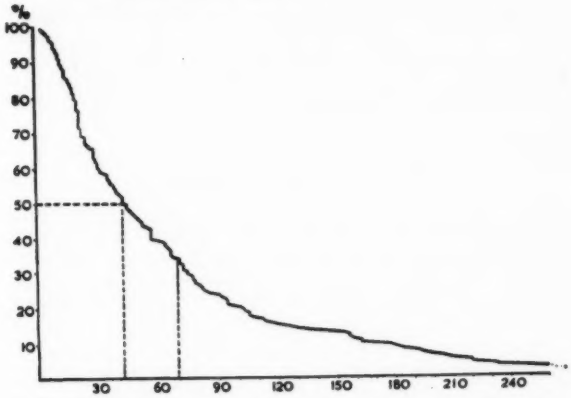
iv. Loss of working time

During the two and a half years' study in the factory clinic, 18 dermatitis patients were away from work for more than three days, corresponding to an incidence of 1.5/1000/year, which approximates to the national average for 1944–46. The time lost by these patients is shown in Table VI,

TABLE VI. WORKING DAYS LOST OWING TO SKIN DISEASE AMONG 5,100 MANUAL WORKERS IN ENGINEERING FACTORY, 1946–48

	Number affected (hands or forearms)	Number away from work	Total time lost (days)	Mean time lost (days)
1946 (12 months)	29	12	776	64.7
1947–8 (18 months)	40	6	139	23.2
	69	18	915	50.8

FIG. 4. TIME OFF WORK IN 175 CASES OF INDUSTRIAL DERMATITIS OCCURRING IN THREE BIRMINGHAM FIRMS (1943–46)



Ordinates: percentage of cases remaining off work at the end o various periods of time

Abscissae: days

Dotted lines indicate median (42 days) and mean (69 days) periods off work

the mean loss per patient being 51 days. As this sample is small and might not be regarded as representative, the records of two other large factories, both with well-equipped medical departments, were combined with this study so that 175 patients could be included. The results obtained are plotted in fig. 4, the mean time loss being 69 days; 50 % of the patients were away from work for more than six weeks and 10 % for more than six months. This situation is clearly very serious; apart from the considerable loss of earnings and production as well as expenditure on compensation and medical treatment, the loss of morale of men incapacitated for more than one or two months is very evident.

Further analysis of the patients away from work in the engineering factory which was studied in detail showed that vesicular rashes were more serious than non-vesicular. Not only was a suggestively higher proportion of these patients forced to stay away from work (11 out of 28 with vesicular lesions as compared with 7 out of 41 with non-vesicular), but the average time lost by patients with vesicular lesions was significantly greater (67 days for vesicular lesions, 26 days for the others—standard error of difference = 14.6 days; "t" test: $P < 0.05$).

A history of previous skin disease was obtained from a relatively small number of patients, and of those off work only one-sixth (3 patients) had any such history and these lost only 134 days—approximately one-seventh of the total time lost. The proportion of the factory population which had any such previous history is not known, but their elimination would have saved only one-seventh of the total time lost. It may, however, be advisable, as suggested by some authors, to prohibit the employment of patients with previous skin disease on jobs which carry a known high dermatitis risk.

There is evidence that the institution of a special clinic for skin cases in a factory with the attendant medical and nursing care leads to a considerable reduction in lost time. The improvement shown in the engineering factory in Table VI was duplicated in a nearby factory by another medical officer.

Consideration of Table VI shows that while the incidence of patients reporting in each period remained constant there was a significant reduction during the last eighteen months in the number of patients away from work, and in the mean duration of their absence. It is impossible to relate this improvement to any one factor but it is likely that it was achieved mainly as a result of the increased interest of the nursing staff and improved methods of treatment.

3. Laboratory Investigations

a. Bacteriology

Legge (1934) has pointed out the frequent importance of coccal infections in the clinical picture of industrial skin disease. As shown in the work reviewed by Stuart-Harris (1948) much remains to be learned of the bacterial flora on normal skin and in various types of skin disease. As a preliminary survey we have examined films of all varieties of colonies growing on blood agar plates from the first lesion swab of about 200 patients. Gram-positive cocci were preponderant both numerically on individual plates and as the type of organism most frequently isolated from different patients. Since many recognized pathogens do not grow well on blood agar plates or might be overgrown, special media of ten different kinds were used to examine in detail the flora of the lesions and of the normal wrist skin of ten patients. No clostridia, diphtheria bacilli, salmonella, acne bacilli or pleuropneumonia-like organisms were isolated from any of the lesions. No examination was made for viruses.

For these reasons it was decided to confine the present study to gram-positive cocci of recognized human pathogenicity—namely *Staph. aureus* (coagulase-positive gram-positive cocci) and streptococci of Lancefield's Groups A, C and G. To this end, the routine media were blood agar plates incubated aerobically and broth incubated anaerobically (Williams & Miles, 1945). Gentian violet media and anaerobic culture on blood agar were frequently used, particularly for swabs from new patients. A few varieties of colonies of gram-positive cocci on the direct plate and all varieties on broth subculture were tested by the coagulase test, and, if the colonial appearance indicated, by Lancefield's grouping. The staphylococci isolated were tested as a routine, by a plate dilution method, for their sensitivity to penicillin. By penicillin-resistant we mean that a small inoculum (5–50 colonies) grew on a plate containing 0.1 unit/ml. penicillin.

Owing to the normal carriage of *Staph. aureus* on the healthy skin, little reliance has been placed on the mere presence of pyogenic cocci on a lesion swab, but attention has been focused on the incidence of pyogenic cocci in lesions of different clinical appearance and site, and the association between carriage on these lesions and on healthy skin and nose. In this way we have attempted to define the role of added coccal infection in industrial skin disease.

The results described, except where otherwise stated, are based on all the patients seen in the light engineering factory, described in section 2, whose lesions were swabbed. These comprised 98 patients—86 manual and 12 non-manual workers.

Streptococci of Lancefield's Groups A, C and G

These organisms were found in the lesions of 11 out of 98 patients. The anatomical sites which were infected with streptococci included the hands and forearms, legs and feet. No special tendency for any one of these sites to be infected with special frequency was noted, though in general the more widespread lesions most frequently became contaminated. The clinical types of lesion most at risk were those which at some time were moist with exudation or serum. Only one out of the 11 patients with streptococcal lesions never exhibited serious oozing. Only two of the lesions were of a nature commonly recognized to be streptococcal; one was an erysipelas, the other an ecthymatous ulcer. The underlying pathology in the remaining cases included trauma such as burns from alkali or welding, local dressing sensitization reactions, fungal skin diseases either localized or producing sensitivity vesicular reactions, and vesicular dermatitis of unknown etiology. In these conditions there is no doubt that streptococcal infection at times leads to an exacerbation of the condition with easily recognizable clinical signs. In these patients, the area showed signs of inflammation with redness, oedema, yellowish crusting and sometimes oozing of frank yellowish-green pus. Axillary adenitis has been seen. In only 4 out of 11 patients was the streptococcal infection " silent " and in these the organisms were often isolated infrequently or in small numbers.

Lancefield's grouping of streptococci from the lesions of an additional 56 patients with dermatitis provided data on the frequency and pathogenicity of each group. Infection by more than one group occurred in 9 out of 67 cases. Of the remaining 58 patients, Group A was commonest (42 cases), and Group C (11 cases) and Group G (5 cases) were in the approximate ratio of 2 : 1. Although marked oedema was not seen except in patients with Group A streptococci, redness, crusting and pus were seen in lesions yielding streptococci of Groups C or G only. These results indicate that pathological effects may arise in skin lesions with added streptococcal infection whether of Group A, C or G.

It is most likely that the added streptococcal infection is derived from the patient's environment by the same routes as those deduced for added streptococcal infection of small wounds (e.g., from other wounds and from throats). Throat swabs of the factory population were not taken as a routine. That the patient's own nose or healthy skin is rarely the primary source of the streptococci is suggested by the recognized low incidence of this organism on these sites in normal individuals, and by the fact that in the factory under investigation no patients out of 87 with lesions free of streptococci yielded streptococci from the nose, and only 1 out of 87 yielded streptococci from the healthy skin. It follows, as previously stressed for the care of small wounds (Clayton-Cooper & Williams, 1945; Gissane, Miles & Williams, 1944), that dressing station hygiene is of importance if industrial dermatitis is not to be needlessly exacerbated.

Once the streptococcal lesion is established other sites may be contaminated. The immediately surrounding skin may yield a heavy growth of the organism. For example, gentian violet blood agar incorporated on sterile gauze and pressed on to the skin demonstrated very large numbers of streptococci over a radius of three inches (7.6 cm.) from the lesion. Further away the numbers were smaller, and streptococci were absent six inches (15.2 cm.) from the lesion. Four out of 30 patients whose streptococcal lesion and wrist skin were swabbed on the same day yielded streptococci of the same group on both sites; the nose under similar circumstances yielded streptococci from 8 out of 35 patients. In at least

TABLE VII. ISOLATION OF STAPH. AUREUS FROM THE FIRST SWABS TAKEN FROM 129 LESIONS IN 98 PATIENTS

Lesions	Numbers of lesions	Isolation of Staph. aureus			
		*		†	Absent
		Number	Percentage	Number	Number
Hand {vesicular ...	22	17	77	3	2
Hand {other ...	16	7	47	2	7
Arm	39	16	41	5	18
Head	20	10	50	3	7
Leg...	32	17	53	2	13
Total	129	67	52	15	47

* = isolated from blood agar plate.
† = isolated from broth subculture only (i.e., very small numbers).

three of these patients the lesion had previously yielded streptococci and the nose had been free, suggesting that lesion-to-nose contamination had occurred. Similar evidence has shown the contamination of one skin lesion by another in the same patient.

In view of these findings it is a reasonable practice to search for possible foci such as small skin lesions and cracks (e.g., at angles of nose or ears), to swab the nose, and to consider chemotherapy not only of the lesion itself but also of the neighbouring skin and any other demonstrable source of streptococci.

Presence of Staph. aureus *in Industrial Skin Disease*

As stated above, very large numbers of *Staph. aureus* were frequently isolated from the lesions of patients seen in the factory clinic. This finding has led to further careful study of the distribution and other aspects of this organism's behaviour.

Analysis of the first swabs taken from the lesions of each patient (Table VII) shows that an abnormally large proportion (52% of the lesions) yielded *Staph. aureus* on direct plate culture, as compared with 27% of those taken from the normal wrist skin of 86 of these patients, and about 20% on this area in the normal population.

Phage typing was attempted on strains of *Staph. aureus* from the skin lesions of 94 patients seen in factory or accident hospital clinics. At one time or another 73 patients yielded strains which could not be typed by phage. Although it is probable that with more concentrated phage suspensions some of those strains could have been typed, the possibility of a preponderant type of staphylococcus lysed by none of the available phages should not be forgotten. In 46 patients a strain which could be typed was isolated on at least one occasion, and the results from these cases are recorded in detail in Table VIII for comparison with data on staphylococci from other sources. The range of types is similar to those isolated in Birmingham from healthy noses and skins of small numbers of patients admitted to hospital with burns or other accidents; many of the types are proved pathogens, the same types having been isolated at operation from finger pulp infections. The slightly increased incidence of types of *Staph. aureus* which frequently produce penicillinase (e.g., type 47) may, as described below, be attributable to local penicillin therapy, but more data are required to test this hypothesis. No one type of skin lesion (e.g., vesiculation, folliculitis) was associated with a particular phage type. In some patients (see, e.g., Table VIII, patients 4, 17, 23, 26, 28, 29, 30, 31 and 36) the same type has been isolated often enough to suggest strongly that the same type or limited number of types is tending to colonize different lesions in the same patient or to persist in the same lesion, often for months.

The staphylococci, in patients not receiving local penicillin, were generally sensitive (cf Table XI). This possibly reflects the low incidence of resistant strains on healthy skin. For example, when 17 patients were swabbed on five different skin sites, only two yielded resistant *Staph. aureus* (one from the finger, one from the shin).

A routine follow-up of individual patients has shown that after healing had occurred, the incidence of *Staph. aureus* fell to a figure approaching that found on normal healthy skin. In a small number of cases remission of lesions was characterized by the same finding, while during exacerbations (particularly in vesicular lesions) isolation of large numbers of *Staph. aureus* was again usual. This association was not constant and it is clear that heavy colonization of the area of the lesion can occur during periods of relative quiescence.

There is evidence that the incidence of *Staph. aureus* is also

TABLE VIII. BACTERIOPHAGE TYPES OF STAPH. AUREUS ISOLATED FROM THE SKIN LESIONS OF 46 PATIENTS YIELDING STRAINS WHICH COULD BE TYPED

	Phage-type group 3A/3B/3C/51		Phage-type group 29/31/52		Phage-type group 6/47		Phage-type group. Miscellaneous	
	Patient	Typing result	Patient	Typing result	Patient	Typing result	Patient	Typing result
20 patients yielding one type only	1	3C(1)	9	52A(1)	13	47(1)	19	42E(1)
	2	3C(1)	10	52A(1)	14	7/47B(1)	20	47A/47B(1)
	3	55(2)	11	52A(1)	15	6/47(1)		
	4	3B/3C/55(5)	12	29(2)	16	6/47(1)		
	5	3B/3C/55(1)			17	6/7(3)		
	6	3C/51/55(1)			18	7(1)		
	7	3B/3C(2)						
	8	3C/51(1)						
16 patients yielding one type* + NT strains	21	3A(1) NT(4)	26	52A(8) NT (6)	29	47(3) NT(2)	36	7/29/47C/52A (4) NT (3)
	22	55(1) NT(3)	27	52A(2) NT (1)	30	47(4) NT(2)		
	23	3C(10) NT (3)	28	31(3) NT (4)	31	47(5) NT(1)		
	24	3A/3B/3C/51(1) NT (3)			32	6/47 (1) NT (2)		
	25	3A/3B/3C/51(1) NT (2)			33	47/47B (1) NT(1)		
					34	47(2) 47B (3) NT(2)		
					35	47 (2) 6/47 (1) NT(3)		

	Patient	Phage types found
10 patients yielding more than one type	37	3C/51/55(1) 47(2)
	38	3A(1) 52A(1) NT(5)
	39	3C/51/55(1) 52A(1) 47B(1)
	40	3C/51/55(6) 52A(3) NT(16)
	41	55(1) 52A(1) 6(1) 47B(1) NT(4)
	42	3C(1) 29(1) 47(3) NT(3)
	43	3C(1) 6(1) 47A(1) 47A/47B(4) NT(4)
	44	3A(1) 7(1) NT(3)
	45	52A(1) 47(1) NT(1)
	46	29(2) 47(1) NT(6)

NT = not typable by available phages.
Figures in brackets indicate the number of occasions on which the type was isolated. Only one colony was tested from each swab.
* Patients Nos. 34 and 35 yielded two types within the same group which suggests that they may be identical.

TABLE IX. IDENTITY OF BACTERIOPHAGE TYPES OF STAPH. AUREUS ISOLATED FROM DIFFERENT SITES OF 17 PATIENTS WHOSE LESION AND A HEALTHY SITE YIELDED AT LEAST ONE STRAIN WHICH COULD BE TYPED

Patient	Nose	Healthy skin sites	Lesion sites
4	3B/3C/55 (1)	3B/3C/55 (3)	3B/3C/55 (5)
11	52A (1)	52A (1) NT (1)	52A (1)
14	—	7/47B (1) NT (1)	7/47B (1)
18	52A (1)	7 (2) 52A(1)	7 (1)
19	—	42E (1)	42E (1)
21	—	3A (3) NT (1)	3A (1) NT (4)
23	3C (6)	3C (4) NT (2)	3C (10) NT (3)
26	52A (1) NT (1)	52A (4)	52A (8) NT (6)
30	47 (1) 47C(1)	—	47 (4) NT (2)
36	NT (1)	7/29/47C/52A(2) NT (2)	7/29/47C/52A (4) NT (3)
37	3C/51/55 (1)	3C/51/55 (1) 47 (2)	3C/51/55 (1) 47 (2)
38	NT (2)	3A (2) NT (2)	3A (1) 52A(1) NT (5)
40	52A (1) NT (2)	3/51/55 (4) 52A(1) NT (5)	3C/51/55 (6) 52A(3) NT (16)
41	6/47 (1) NT (1)	6 (1)	55 (1) 6(1) 6/47B(1) 52A (1) NT (4)
43	—	31 (1) 47A(1) 47A/47B (3)	3C (1) 6(1) 47A (1) 47A/47B (4) NT(4)
44	3A (1) 7 (1) NT (3)	3C/51/55 (1) NT (1)	3A (1) 7 (1) NT (3)
46	29 (2) NT (4)	29 (1) NT (3)	29 (2) 47 (1) NT (6)

NT = not typable with available phages.
Figures in brackets refer to number of occasions on which type was isolated. Only one colony was tested from each swab.

affected by the site of the lesion, the moistness of the lesion, and the presence of vesiculation. It can be seen from Table VII that the hands yield *Staph. aureus* more frequently than any other site, and that this preponderance is largely contributed to by vesicular lesions. Vesicular lesions almost invariably pass through a stage of moistness as vesicles rupture. In such moist vesicular lesions *Staph. aureus* has, without exception, been isolated in large numbers when the patient has first been seen. Examination of the data reveals, however, that in non-vesicular lesions also, the moist lesion is more likely to yield *Staph. aureus* than the dry lesion. Thus in 160 instances note was taken at the time of swabbing as to whether the non-vesicular lesion was moist or dry. Of 60 moist lesions, 50 swabs yielded *Staph. aureus* on the direct plate (83%) while of 100 dry lesions only 53 were positive. More detailed analysis shows this trend to exist for all sites and all types of lesions.

There is ample evidence that there is a close association between carriage of *Staph. aureus* on the lesion, the neighbouring skin, other skin sites and the nose. The figures for nose and lesion carriage are shown in Table X, while inspection of Table IX shows that the same phage type has frequently been isolated from different sites in the same patient. It appears that skin lesions, especially of the hands, are frequently contaminated from the patient's own nose; this result is to be expected in view of the proved contamination of the skin by the nose in normal individuals (Moss *et al.* 1948). The fact that the incidence of carriage by the nose is abnormally high in patients having skin lesions infected with staphylococci might be held to suggest that contamination of the nose from the lesion is also frequent; the association has already been demonstrated for streptococcal skin lesions. This hypothesis of cross-contamination is difficult to prove, but is to be expected, and would explain the results obtained.

There is no doubt that in the factory under study *Staph. aureus* (of multiple phage types and occasionally resistant to penicillin) tended to colonize heavily vesicular rather than non-vesicular lesions, moist rather than dry lesions, hand lesions rather than other sites. Whether this heavy colonization was altering the clinical syndrome is discussed below.

Infection of Moist Skin Lesions

Str. pyogenes is hardly ever found on normal skin; *Staph. aureus* is fairly frequent in small numbers, but disappears after two to three days if the area is protected from outside contamination (Bull, Squire & Topley, 1948). The mechanism by which the normal skin is kept free from these organisms has been investigated intensively during the last two years and the following hypothesis is based on in vivo and in vitro experiments (Burtenshaw, 1948; Ricketts, Squire & Topley, unpublished). Normal skin is coated with a lipid film $\frac{1}{2}$–1 μ in thickness, which consists of sterols (10%), other neutral lipids including glycerides (50%) and fatty acids (40%). About half of the last named are unsaturated long chain fatty acids, including oleic acid. Such acids are strongly bactericidal for *Str. pyogenes*, and to a less extent, for *Staph. aureus*, normal skin resident organisms such as micrococci being more resistant. The bactericidal action of this lipid coat is clearly only one of its functions. Though under normal circumstances the sterilizing power of the unsaturated long chain fatty acids is efficient against potentially pathogenic gram-positive cocci (though at varying rates) their action is inhibited in the test tube and on the skin by serum or serum albumin. Other inhibitors are also known. A satisfactory explanation is thus afforded for the frequent contamination of lesions which allow the escape of serum on to the skin surface.

All the results recorded above could be explained by the expected chances of nose, skin and environmental cross-contamination combined with a reduction in the ability of an area of serum-soaked dermatitis to exert its normal self-sterilizing action against pyogenic cocci. Once established, the pathogenic effects of *Str. pyogenes* are often plain, and have been described above. The possible pathological effects of *Staph. aureus* on lesions of the skin surface are not as clear, similar

TABLE X. ASSOCIATION BETWEEN NOSE AND LESION CARRIAGE OF STAPH. AUREUS (MORE MARKED FOR LESIONS OF THE HAND THAN FOR OTHER REGIONS)

	Nose : *Staph. aureus*		Total swabs	*Staph. aureus* present
	Present	Absent		
Hand lesions				
Staph. aureus present ...	46	7	53	87%
absent ...	6	15	21	29%
Total swabs	52	22	74	
Percentage present ...	88	32	$\chi^2=16.8$ $P<0.001$	
Other lesions				
Staph. aureus present ...	77	32	109	71%
absent ...	38	43	81	47%
Total swabs	115	75	190	
Percentage present ...	67	43	$\chi^2=9.93$ $P<0.01$	

Absent = *Staph. aureus* not isolated from blood agar plate or from broth subculture.

difficulties arising whenever large burns, cuts or other forms of trauma are considered. Clayton-Cooper & Williams (1945) have suggested that delayed healing may be a consequence of "silent" infections of industrial wounds. The development of frank sepsis was more common in wounds contaminated with *Staph. aureus* at the time of infliction than in pathogen-free wounds, and often occurred in wounds from which *Staph. aureus* was the only pathogen isolated from the pus. In our series, frank pus occurred extremely rarely in lesions from which *Staph. aureus* was the only potential pathogen isolated. The signs of redness, exudate, and scaling are too variable and indefinite for precise association with staphylococcal colonization to be possible. It is even more difficult to prove or disprove possible effects of this organism in promoting vesicle formation. Cultures of unruptured vesicles seldom led to the recovery of the organism even when the overlying skin surface was heavily colonized, and cell counts of vesicular fluids seldom showed a high proportion of polymorphonuclear leucocytes. From experience with vaccinia in animals, Lack (1948) has shown that a larger yield of vesicular fluid tended to follow infection with staphylococci (which, as is usual with coagulase positive strains in man, produced hyaluronidase). Until more is known of the precise mechanism of vesicular and other skin reactions or of their evolution in the absence of staphylococcal contamination (which might be observed after therapeutic applications and effective isolation of the area), further discussion of possible inter-relationships is not profitable. It should however be emphasized that vesicular lesions of the hand stand out as almost invariably yielding *Staph. aureus* continually and in large numbers. The chances that a careful investigation would demonstrate more clearly the role of this organism in the disease are perhaps higher for this than for any other non-purulent skin lesion.

Local Penicillin Therapy

Since a high proportion of patients with industrial skin disease was found to carry potentially pathogenic organisms in their lesions, the effects of local chemotherapy were studied. It was hoped to promote more rapid healing and return to work, or at least, by reducing the carriage of organisms, to define their role more accurately. Rapid healing was achieved in many patients using penicillin cream but, as a parallel control series was not instituted, the value of chemotherapy as such could not be proved. Although complete elimination of pyogenic cocci was sometimes achieved, a reduction of their numbers only was a more common finding. Penicillin cream, made up usually in a base of lanette wax S.X. but occasionally in tragacanth jelly or eucerin, was used in a strength of 400–1,000 units/g. and applied daily by factory or hospital nursing staff trained in the principles of avoiding added infection. Bacteriological sampling of the lesion was usually carried out weekly, the swabs being immediately transferred to media containing penicillinase in amounts proved to be sufficient to neutralize any likely quantities of contaminating penicillin. The value of chemotherapy or chemoprophylaxis is critically discussed by Stuart-Harris (1948) and must be finally judged on clinical criteria. Effectiveness may also be considered in terms of the elimination or reduction in numbers of micro-organisms, and it is possible that mere reduction in numbers may result in clinical improvement. As stressed by Cook, Jebb & Knox (1949) it is possible that relatively large numbers of a particular pathogen (throat streptococci) are more likely to be associated with clinical signs than a smaller yield of organisms.

Streptococci of Lancefield's Groups A, C or G were eliminated within two weeks from the lesions of about half the patients with dermatitis, by penicillin applied locally, a finding which is in general agreement with current experience in the similar treatment of infected burns. Earlier experience (Colebrook, 1943) had suggested a higher success rate. Clinical success (disappearance of oedema, pus, crusts) was similarly achieved in about half of the dermatitis patients. A possible reason for occasional failure of penicillin lies in the accompanying colonization of the lesions with penicillinase-producing staphylococci (Cruickshank, Squire & Topley, 1948). The prophylactic value of local penicillin in reducing the risks of streptococcal infection is suggested on theoretical grounds and has been proved for burns (Lowbury and Topley, unpublished observations).

Staphylococcal infection was apparently eliminated in less than one quarter of patients studied during treatment lasting two or more weeks. The commoner finding was a reduction in numbers so that the organism was isolated only on broth subculture. Thus in terms of primary isolation of *Staph. aureus* on the direct plate, out of 29 patients all of whose lesions yielded *Staph. aureus* when local penicillin therapy was started, 11 (38 per cent) yielded no *Staph. aureus* one week later. With more prolonged treatment *Staph. aureus* was reduced on a few more lesions. Clinical improvement was usually noted by the end of the first week, if at all; it was occasionally marked (in perhaps 8 out of 34 patients) but the signs indicating improvement were less definite than in the case of the clinical infection with streptococci. Again it must be emphasized that control observations (e.g., using a cream base alone) were not made.

The possible disadvantages of local penicillin therapy include general sensitization (observed in only one patient) or local effects. It is impossible to define the part played by local penicillin in the occasional exacerbation of the clinical signs of infection during therapy. It is probable that the pustular folliculitis that occasionally occurs round an area of dermatitis may be caused by the lanette wax or eucerin base. Certainly the replacement of lanette wax by a tragacanth base has, in individual patients, resulted in disappearance of the surrounding folliculitis, and such a folliculitis appears to be extremely rare if the tragacanth base is used from the onset of treatment.

Penicillinase-producing staphylococci may be responsible for clinical failure in treating staphylococcal or streptococcal infection (see above). More than 90 % of penicillin-resistant staphylococci actively produced penicillinase (a 24-hour broth culture destroyed 30 units/ml. penicillin within three hours) and when heavily colonizing a lesion they are probably capable of destroying within a few hours all the penicillin contained in a few grams of the preparation used on the skin. The actual rate of disappearance of penicillin cannot be defined as there is at the moment no accurate micro-technique available to analyze penicillin extracted from the skin surface. Certainly penicillin-resistant *Staph. aureus* as described above are normal, though uncommon, inhabitants of the healthy skin and nose. They may colonize a lesion during penicillin therapy. For example, of 14 patients who had not received penicillin at the time of swabbing, only three carried penicillin-resistant *Staph. aureus*, whereas 10 out of 20 patients harboured penicillin-resistant organisms at one time

TABLE XI. ASSOCIATION BETWEEN THE PRESENCE OF PENICILLIN-RESISTANT STAPH. AUREUS IN SKIN LESIONS AND LOCAL PENICILLIN THERAPY

	Patients never having local penicillin therapy		Patients during or within one month after local penicillin therapy	
	Lesion staphylococci never resistant	Lesion staphylococci resistant on one or more occasions	Lesion staphylococci never resistant	Lesion staphylococci resistant on one or more occasions
Engineering factory patients	11	3	9	10
Other patients ...	15	5	11	10
Total	26	8 (24%)	20	20 (50%)

$\chi^2 = 4.4$
$P < 0.05$

or another after the onset of local penicillin treatment. Including further cases of dermatitis seen in factory and accident hospital clinics this difference becomes statistically significant (Table XI).

Other possible causes of failure include inadequate dosage and continual contamination of the lesion from other sites. As shown above, the neighbouring skin, remote skin sites, and the nose are likely to be contaminated frequently with staphylococci and less commonly with streptococci. This suggests the risks to which the area of dermatitis is itself secondarily exposed. Treatment of these contaminated sites with penicillin is possibly indicated, e.g., by spraying the nose (Hobbs, Carruthers & Gough, 1947; Moss *et al.* 1948), and by including a wide area of healthy skin in the local dressings.

It appears that local chemotherapy in certain types of industrial skin disease, which in our experience is usually associated with the presence of pyogenic cocci, may reduce the period of disability. Further investigations using penicillin and other new drugs are indicated.

b. Other Pathological Investigations

In addition to the more detailed bacteriological investigations described above, special clinical pathological tests were used on several of the patients when indicated by the clinical appearances. Cases of suspected epidermophytosis were confirmed, or otherwise, by examination of scrapings from the lesion by the direct film method and by culture. Of the 123 patients in this series, 33 were examined in this way, with positive results in eight. Trichophytin skin tests were occasionally valuable in confirming fungal sensitization. Specific patch tests were performed on small scarified skin areas to confirm suspected dressing sensitivities, and to establish precisely the offending agent.

Blood eosinophils were enumerated when sensitivity reactions were noted either secondary to fungal infection or as a result of exposure to sensitizing agents. Of the 33 eosinophil counts performed, only one showed a deviation from normality, and this patient was shown to have been suffering from fungal infection of the feet with associated trichophytid reaction. The absence of abnormally high eosinophil counts among such a high proportion of the patients examined suggests that, in this factory, disseminated sensitization reactions were not a common occurrence (Cruickshank & Squire, 1949). The haemoglobin level and the white blood cell count were also estimated where any deviation from the normal was suspected, but this was seldom found. In a few isolated instances, blood sedimentation rates were examined —again mainly giving normal results. Wassermann reactions were performed on eight patients and in one instance tertiary syphilis was detected.

A sample of urine from each patient was tested as a routine. The findings were usually normal, though the discovery of diabetes in one patient with chronic pruritus indicated the value of this testing.

4. Prevention and Treatment

Much has been written about the prevention of industrial dermatitis, and much sound advice given. Especially important are the steady improvement in factory hygiene and the increased facilities for cleanliness which are seen in many modern factories. But our studies have emphasized the diversity of the factors contributing to dermatitis even within a single factory, and evidently no single panacea can be effective. We would recommend a careful list to be kept by each factory clinic or first-aid worker of all cases of skin disease of hands and forearms, whether mild or severe. The list should include a record of the worker's job and shop. The numbers reporting should be compared regularly with the populations working in various jobs or shops, and any undue incidence should be investigated immediately. Industry is never static; new personnel, new methods and compounds are constantly being introduced. A new worker may immerse his hands in caustic; a new adhesive may contain excess of formalin as preservative; a new anti-rust compound may contain a sensitizer. The problem is different on each occasion, but it can usually be identified by a combination of medical and engineering knowledge. Specific prophylactic measures, even protective clothing, may be needed, but wherever practicable, substitution of safe compounds and methods and improved hygiene should be the rule. H.M. Medical Inspectorate of Factories can give invaluable help, and occasionally a consultant dermatologist may be needed. The key to each problem is adequate information and the list suggested above supplies this.

The value and choice of cleansing agents may need careful study. Cruickshank (1948) has shown that there are considerable differences between various substances in their power to free the skin from oil, as well as in their effectiveness if used correctly. Use was made of the fluorescence of mineral oils which could be seen even in small amounts on the skin and in the mouths of the hair follicles. Barrier creams appeared to be of little value against oil, though replacement of natural skin fats by lanoline mixtures after washing with powerful agents was recommended. Similar methods should be useful to industrial medical officers, both for testing the value of washing and other protective measures, and when teaching workmen the importance of adequate cleansing.

The treatment now given to patients with industrial skin diseases could be greatly improved. Our experience leads us to advocate the institution of a weekly clinic specially reserved for medical supervision of the diagnosis and treatment of industrial skin disease in all large factories. The treatment ordered can then be carried out daily by the factory nurse. For lesions such as erythema without serous oozing, simple

gentle cleansing and soothing applications such as the traditional calamine lotion have been effective. Vesicular or oozing lesions raise the same problems as the open wound, perhaps in even more serious form—the prophylaxis and treatment of added infection. Strict no-touch techniques must be employed. The evidence for the value of chemotherapy, though probably the ideal agents remain to be discovered, has already been set out. Recurrent vesicular and other lesions may call for the advice of the consultant dermatologist, and there is little doubt that some severe rashes are most effectively treated in hospital.

The risk of sensitization to medical preparations should constantly be borne in mind by medical and nursing staffs. On this account, sulphonamides are best avoided for local applications on the skin; at present, sulphathiazole powder is still frequently used as a diluent for penicillin which is to be insufflated into wounds. Thermal or alkali burns are still too frequently complicated by reactions to picric acid, acriflavine, or even to cetrimide, though the risk of sensitization may be considered to be worth while with useful preparations like cetrimide and penicillin cream.

Whether a man should be advised to cease working, to return to, or to change his job should be decided on the basis of a knowledge of the factors leading to the attack of skin disease. The key list to be kept by each factory as previously mentioned and the carefully taken history of the patient in the clinic are valuable adjuncts. Considerable damage can be done by sending a worker who has suffered from a severe sensitization rash back into contact with the offending chemical. Similarly, a man who has been mishandling an acute irritant or caustic should not be allowed to go on harming himself without instruction in methods of avoiding the hazard. On the other hand, many patients subsequently carry out the same job without fresh trouble, and the great loss of earnings and status which may result if, say, a skilled tool-setter is degraded into a storeman or cleaner should be avoided wherever possible. The most balanced decision is made by the keen well-trained industrial medical officer, and although many problems of organization are involved, the ideal of a medical service for each factory, even the smallest, should be held in mind.

Of further research there is still great need. Well documented clinical studies like those of Goldblatt (1945) and Jones (1946) are very valuable in disclosing fresh hazards or defining problems such as those of a chemical factory. Following these, technical research is frequently required to discover compounds with similar usefulness, but with less danger to the user. Constant statistical appraisal of the situation in the country as a whole and in particular industries is needed, and the future reports of the new Ministry of National Insurance are keenly awaited. Further bacteriological investigations should lead to more effective control, at least of secondary infections. The salient problems for the experimental pathologist appear to be the mechanism of sensitization of the skin and of vesiculation in general. Sensitization can be well studied in animal experiments (Landsteiner, 1947; Sulzberger, 1940; Gell, 1944; Gell, Harington & Rivers, 1946), though so far many agents which are known to sensitize man fail to give convincing reactions in readily available laboratory animals. The vesicular reaction has been studied using histological methods by many workers (see Percival & Hannay, 1949; Polak & Mom, 1949) but much remains to be learned of the underlying biochemical reactions. If the vesicular reaction could be stopped in its tracks, as the urticarial weal reponds to the antihistamine drugs and the Lewisite burn to BAL, much loss of wealth and happiness could be prevented.

ACKNOWLEDGEMENTS

It is a pleasure to thank all those who have helped in the work we have described: Dr J. M. Davidson, Ministry of National Insurance; Dr J. E. Cottrell, Dr S. Horner, Dr E. R. A. Merewether, of the Factory Department, Ministry of Labour and National Service; Dr E. H. Capel and Dr J. G. Lawson, and many other industrial medical officers; Dr J. P. Bull, Dr C. R. Ricketts, Mr A. M. Hood and other members of the Medical Research Council Units in the Birmingham Accident Hospital.

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COALMINERS' PNEUMOCONIOSIS

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Coalminers' pneumoconiosis has been one of the most serious problems in industrial medicine in Great Britain during the past 20 years. The disease was described both clinically and pathologically over 100 years ago by Thompson (1836), but during the latter part of the nineteenth century and the first twenty years of the twentieth century the disease was generally thought to have disappeared, presumably owing to improved conditions in the mines (Collis, 1915). However, during the third decade of this century reports began to appear, more especially in South Wales, of pulmonary abnormalities in coalminers, resembling those seen in silicosis (Tattersall, 1926; Welsh National Memorial Association, 1931; Harper, 1934). In 1930, Cummins & Sladden published a detailed account of the pathology of such cases, describing it as a form of silicosis modified by accumulation of coal dust.

Coalminers with silicosis first became eligible for compensation under the Workmen's Compensation Act of 1929. At first, only a limited number of men employed in certain work were admitted to compensation, but in 1934 all underground workers in coalmines became eligible and the steadily increasing number of men who were certified as having silicosis by the Silicosis Medical Boards, especially in South Wales, showed that the disease was widespread there (Table I). During the same period, the appearance among coalminers of anthracosilicosis, as it was generally called, began to be reported in various countries: Germany (Boehme, 1925); Sweden (Edling, 1926); Australia (Badham & Taylor, 1933); France (Magnin, 1935); Belgium (Langelez, 1938); America (Bloomfield *et al.* 1935; Flinn *et al.* 1941); and USSR (Moshkovsky, 1941).

1. Reports from Committees on Industrial Pulmonary Diseases

In 1937, the Industrial Pulmonary Diseases Committee of the Medical Research Council initiated an investigation into chronic pulmonary disease among coalminers in South Wales. The results were published in the Medical Research Council's Special Report Series, Nos. 243, 244 and 250. In the first of these reports Hart & Aslett (1942) presented the results of their clinical and radiological survey of coalworkers in South Wales; in the second part of the report Belt & Ferris (1942) gave an account of the pathological changes seen in these men's lungs. Hart & Aslett showed that there was widespread pulmonary disease in workers exposed to coal dust in the mines of South Wales, and also among the coaltrimmers who load commercial coal into the holds of ships in South Wales ports. Men exposed to rock dust in the mines were more prone to develop pulmonary disease than men working only on the coalface, but since a far greater number of the latter were employed in the industry they provided most of the cases in South Wales. Since the disease was more prevalent in anthracite mines than in bituminous mines, with semi-bituminous or steam-coal mines occupying an intermediate position, Hart & Aslett suggested that the incidence of the disease was in some way related to the rank[1] of coal that was mined.

The radiological abnormalities described by Hart & Aslett started with a condition which they named "reticulation", a term which has caused some confusion and which is tending to be abandoned; for in the earlier stages of the disease good radiographic technique reveals fine mottling from the onset, rather than a reticular pattern (Fletcher *et al.* 1949). The

[1] The "rank" of a coal is roughly inversely proportional to the amount of volatile matter it contains. In South Wales, anthracite coals with less than 5% volatile matter have the highest rank, and bituminous coals with over 30% volatile matter have the lowest rank.

TABLE I. NUMBER OF NEW CASES OF SILICOSIS AND PNEUMOCONIOSIS AMONG COALMINERS CERTIFIED ANNUALLY BY THE SILICOSIS MEDICAL BOARDS IN GREAT BRITAIN

Year	South Wales coalfield			All other coalfields in Great Britain		
	Partially disabled	Totally disabled	Annual total	Partially disabled	Totally disabled	Annual total
1931	14	30	44	—	—	—
1932	30	69	99	—	—	—
1933	61	123	184	10	8	18
1934	45	135	180	14	5	19
1935	53	139	192	21	15	36
1936	71	214	285	19	4	23
1937	93	156	249	25	17	42
1938	155	228	383	29	15	44
1939	228	177	405	21	23	44
1940	272	160	432	12	21	33
1941	327	158	485	15	19	34
1942	485	260	745	26	28	54
1943	823	302	1125	91	50	141
1944	1303	255	1558	315	128	443
1945	4651	529	5180	422	152	574
1946	3405	348	3753	455	145	600
1947	2474	322	2796	634	240	874
Total	14490	3605	18095	2109	870	2979

later stages of the disease described by Hart & Aslett were very similar to silicosis. There was nodulation which tended to become confluent, with the ultimate formation of massive shadows. Hart & Aslett concluded that these varying radiological abnormalities represented a continuous pathological process and suggested that tuberculosis, although it might be associated with the disease, did not play a causative role. Belt & Ferris described the development of reticulin fibrosis, which they attributed to the presence of silica, in lungs which had a radiological appearance of " reticulation ". They suggested that when collagenous fibrosis occurred either in the form of nodules or as areas of massive fibrosis it was due to the dust, but that tuberculosis was often a contributing factor.

The second report of the Medical Research Council, No. 244, gave the results of various investigations into the quantity and quality of air-borne dusts in the mines of South Wales (Bedford & Warner, 1943; Briscoe *et al.* 1943; Nagelschmidt, 1943). The general conclusion supported Hart & Aslett's contention that anthracite dust was more harmful than lower-rank coal dust. Tentative levels were suggested for dust concentrations that would not be expected to give rise to pulmonary disease.

In the Medical Research Council's third report, No. 250, King & Nagelschmidt (1945) reported on chemical analyses of lungs of South Wales coalminers, and showed that coalminers who had worked in rock and had the classical silicotic type of nodulation had a higher quartz content in the lungs than those who had worked at the coalface and had reticulin or massive fibrosis. In the latter cases, although all the lungs contained abnormal amounts of quartz, there was no significant correlation between either the amount of coal or quartz in the lungs and the degree of fibrosis. In the same report, Belt & King (1945) reported on animal-inoculation experiments in which South Wales coalmine dusts were found to have little fibrogenic action except when the proportion of quartz and mica was high.

2. New Compensation Scheme

Following these investigations of the Medical Research Council, an intensive dust suppression campaign was initiated in the mines of South Wales. In 1943, a new scheme for compensation was introduced under the Workmen's Compensation Act which admitted men who showed the radiological appearance described by Hart & Aslett (1942) as " reticulation ". In the succeeding years, the numbers of men certified with coalminers' pneumoconiosis in South Wales increased rapidly (Table I). This increase was chiefly due to the altering of diagnostic standards for certification, but in addition there is evidence that there was a true increase in the prevalence of the disease in the late nineteen-thirties and that various social and economic factors led more men to apply for compensation (Fletcher, 1948). In the rest of Great Britain there was also an increase in the number of certifications, but the numbers remained very much lower than in South Wales, and throughout the whole period 1930–48, for which figures are available, the prevalence of the disease was forty times as great in South Wales as in the rest of the country. The seriousness of the problem in South Wales, where during this period nearly 20,000 men were certified, requires no emphasis either from the medical point of view or from the point of view of loss of man-power and financial cost in compensation. Moreover, all the certified men were suspended from further work in the coalmining industry and had to seek alternative employment in an area where unemployment was already at a high level. A large number of men had to bear the burden of unemployment in addition to the disability caused by the disease.

3. Recent Investigations

In 1945, the Medical Research Council set up a Pneumoconiosis Research Unit in South Wales to enquire into every aspect of the problem presented by this disease. The state of knowledge at that time, concerning the disease, may be very briefly summarized as follows. It had been demonstrated that pulmonary disease attributable to the inhalation of coal dust was widely prevalent among the coalminers in South Wales. Its prevalence appeared to be related in some way to the rank of coal that was mined and it was thought that both silica and some unspecified factor (probably tuberculous) were mainly responsible for the development of pulmonary fibrosis.

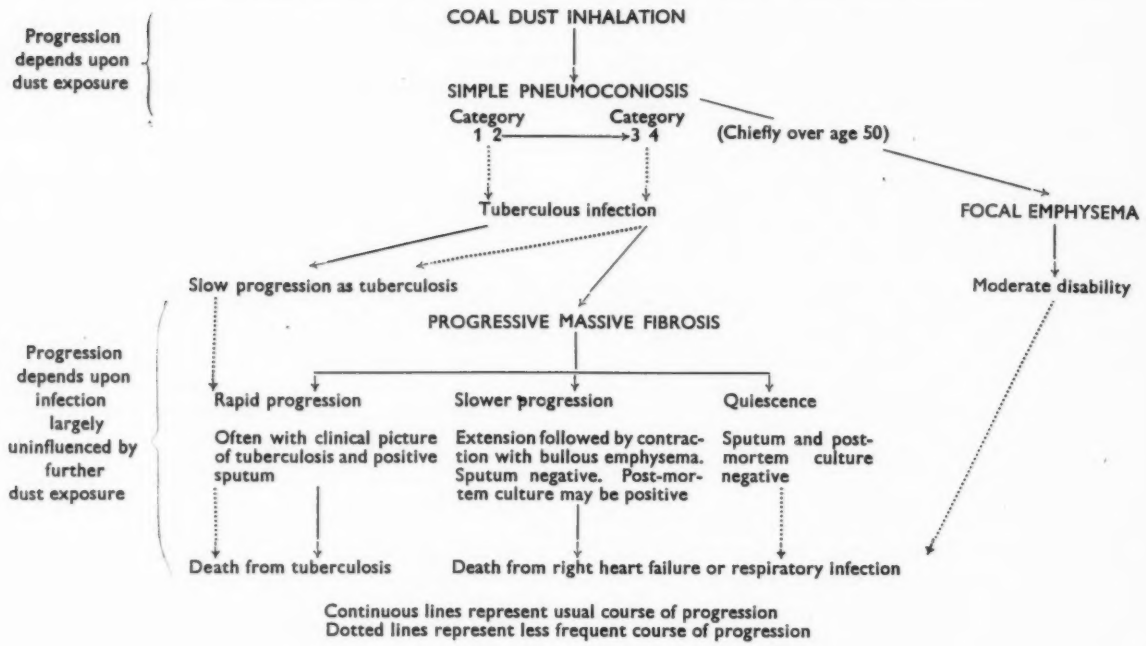
a. Pathological Findings

Meanwhile, however, Gough (1947), working in the Welsh National School of Medicine, Cardiff, had suggested that from the pathological point of view there were two distinguishable disease processes involved. In the first, simple pneumoconiosis, inhaled coal dust accumulated in small deposits or foci (Plate V, fig. M) in the lungs and gave rise to a small amount of reticulin fibrosis. Later, the surrounding alveoli tended to break down to form emphysematous spaces, an appearance which was termed focal emphysema (Plate V, fig. N). Focal emphysema is more frequently found, and is of greater severity, in coalworkers' pneumoconiosis than in classical silicosis (Plate V, fig. O). Gough (1944) suggested that this emphysema might be the cause of disability in the simple type of the disease. A detailed account of the development of these small deposits of coal has been given by Heppleston (1947). The second disease process, described by Gough as infective pneumoconiosis, was one in which he was confident that tuberculosis played an important part. In it, collagenous fibrosis developed in and around the coal foci to form " infective nodules " (Plate V, fig. P) which later tended to fuse and form the massive areas of fibrosis characteristic of the later stages of the disease (Plate VI, fig. Q). Tuberculous infection might also result in diffuse fibrosis occurring between the coal foci. Death was frequently due to right heart failure and, less often, to active tuberculosis, thus differing from classical silicosis. Gough (1940) also showed that the pathology of coaltrimmers' disease was identical with that of coalminers' and since coaltrimmers are exposed only to the dust of commercial coal this dust must be regarded as fibrogenic. The finding of the disease in the men working in ships disposed of previous theories that exposure to fumes of explosives, or long cold journeys underground, might be responsible for the common respiratory disability in coalminers.

b. Radiological Findings

The first studies of the Pneumoconiosis Research Unit were concerned with the radiological follow-up of large numbers of coalminers who had had a previous chest radiograph taken and who had subsequently either remained at

FIG. 1. DIAGRAM OF PROGRESSION IN COALMINERS' PNEUMOCONIOSIS


Progression depends upon dust exposure
COAL DUST INHALATION
SIMPLE PNEUMOCONIOSIS
Category 1 2
Category 3 4
(Chiefly over age 50)
Tuberculous infection
FOCAL EMPHYSEMA
Slow progression as tuberculosis
Moderate disability
PROGRESSIVE MASSIVE FIBROSIS
Progression depends upon infection largely uninfluenced by further dust exposure
Rapid progression
Slower progression
Quiescence
Often with clinical picture of tuberculosis and positive sputum
Extension followed by contraction with bullous emphysema. Sputum negative. Post-mortem culture may be positive
Sputum and post-mortem culture negative
Death from tuberculosis
Death from right heart failure or respiratory infection

Continuous lines represent usual course of progression
Dotted lines represent less frequent course of progression

work, exposed to coal dust, or who had left the mines after certification and had no further exposure. By comparing the first and second radiographs, it was possible to assess the progress of the disease with and without exposure to the inhalation of coal dust. The results of these studies (Stewart, 1948; Davies *et al.* 1949) gave strong support to Gough's conclusions based on pathology.

In men with normal *x*-ray findings and exposed to the inhalation of coal dust, the first radiological abnormalities to appear are minute opacities up to 1 mm. in diameter (Plate VI, fig. R); these increase in number and size, and to a certain extent in radiological density, until the whole of both lung fields is thickly covered with opacities ranging up to 3 or 4 mm. in diameter, which are usually composed of aggregates of the minute opacities (Plate VI, fig. S and Plate VII, fig. T). This condition is termed " simple pneumoconiosis " and it is in itself non-progressive, so far as the radiological appearance is concerned, after dust exposure has ceased. The opacities correspond to the disseminated coal foci described by Gough (Gough, James & Wentworth, 1949). The various degrees of severity are classified radiologically into four categories of increasing abnormality (Fletcher *et al.* 1949).

In certain cases, usually with simple pneumoconiosis of at least the third category, an additional type of radiological abnormality is apparent. This consists of localized, more homogeneous opacities of larger size, which commonly appear in the upper zones, particularly on the right side (Plate VII, fig. U). These nearly always progress, whether or not dust exposure is continued, towards the formation of large massive shadows which later tend to contract, with gross distortion of the lung field (Plate VII, fig. W). This condition has been termed " Progressive Massive Fibrosis " (P.M.F.) and it corresponds to the infective nodules and collagenous fibrosis described by Gough. The combination of " simple " pneumoconiosis and P.M.F. is termed " complicated " pneumoconiosis. The various stages of complicated pneumoconiosis are also classified into four categories, A, B, C and D. The tendency of cases with simple pneumoconiosis of the third or fourth category to develop P.M.F. and the tendency of P.M.F. to progress appears to be uninfluenced by further dust exposure (Davies *et al.* 1949).

In a radiological study of tuberculous shadows in miners with simple pneumoconiosis Mann (unpublished observations) found suggestive evidence that in cases of simple pneumoconiosis of the first and second categories there is an increased incidence of tuberculosis but a slower development of the disease than in non-miners. In cases of simple pneumoconiosis of the third and fourth categories, the tuberculosis appears to be modified so as to form progressive massive fibrosis. Other evidence that progressive massive fibrosis is tuberculous in origin is provided by bacteriological findings (Rogers, 1946; James, unpublished observations) and by the fact that P.M.F. in its active state is associated with a raised sedimentation rate (Stewart, 1948).

Our present conception of pneumoconiosis is (fig. 1) that the inhalation of coal dust leads to the development of coal foci and the associated radiological appearance of simple pneumoconiosis. The presence of coal dust in the lung in some way modifies a tuberculous infection so as to render it more fibrotic. In early cases of simple pneumoconiosis this does not matter, but when there is sufficient accumulation of coal, then the fibrous reaction becomes so intense that masses of collagenous fibrosis occur, occupying and distorting large areas of the lung.

COALMINERS' PNEUMOCONIOSIS

(FIGS. M—W)

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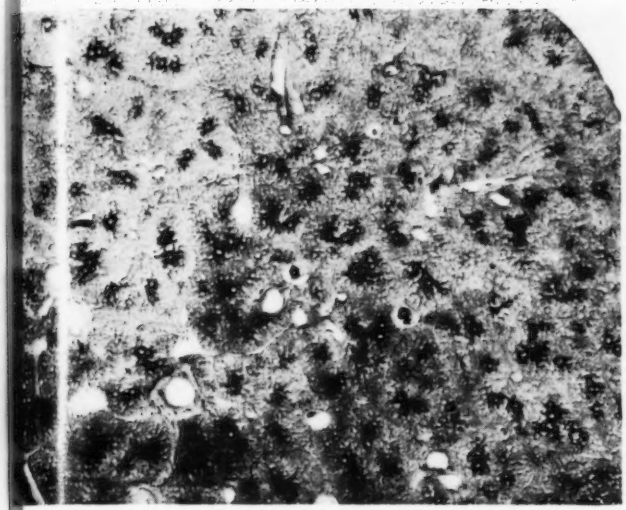

FIG. M. Simple pneumoconiosis in a steam-coal collier. Dust has collected around the smaller bronchioles (magnification × 1½)

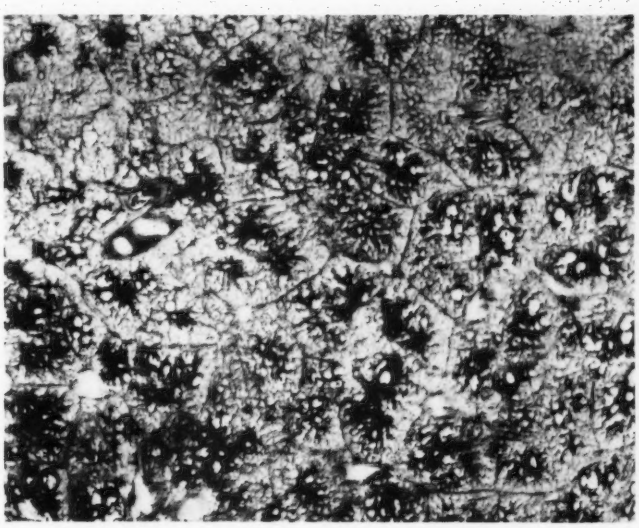

FIG. N. Simple pneumoconiosis with focal emphysema in a coal tipper (magnification × 1½)

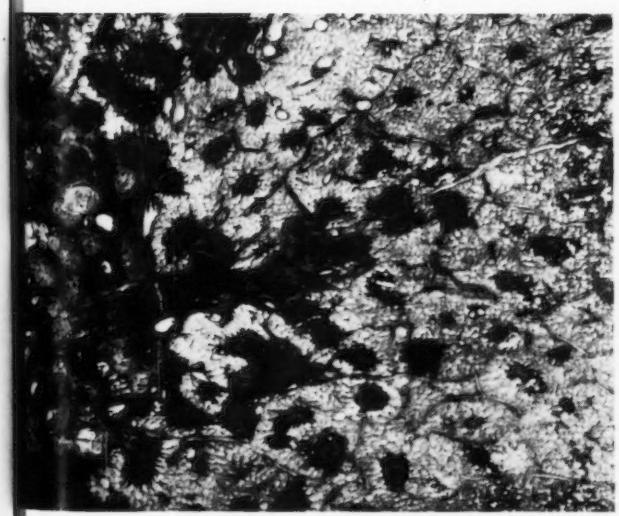

FIG. O. Classical silicotic nodules in a coalminer who had been engaged in drilling rock for 18 years (magnification × 1½)

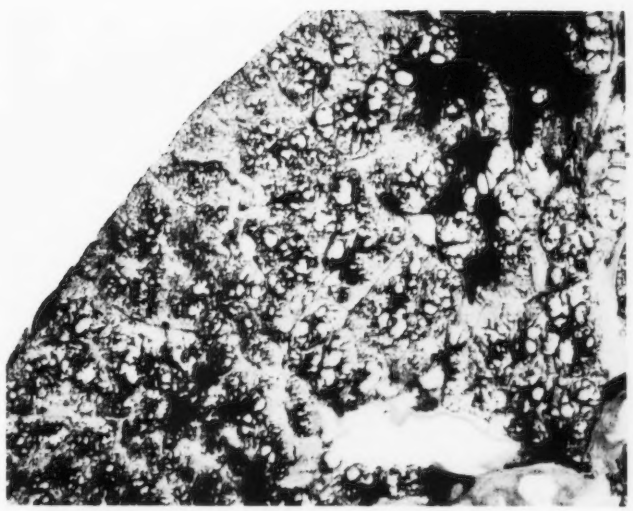

FIG. P. Simple pneumoconiosis, with focal emphysema, and dense confluent nodules due to infection. From a man who had worked as a collier for 50 years in steam-coal mines (magnification × 1½)

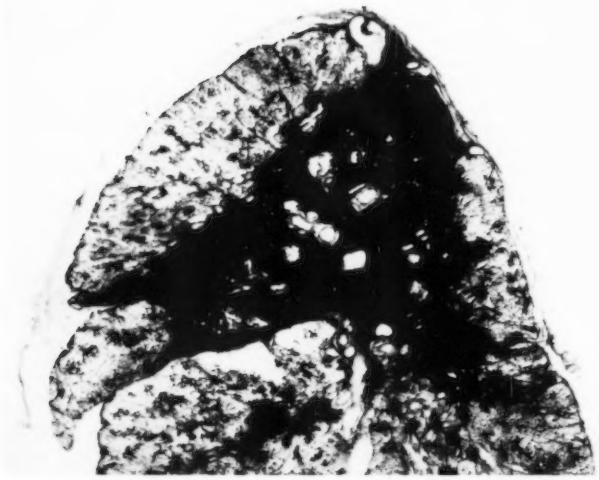

FIG. Q. Massive pneumoconiosis in the upper half of the lung of a collier who had worked for 22 years in steam-coal mines. This type of lesion is regarded as resulting from the combined action of dust and tuberculosis (magnification × ⅓)

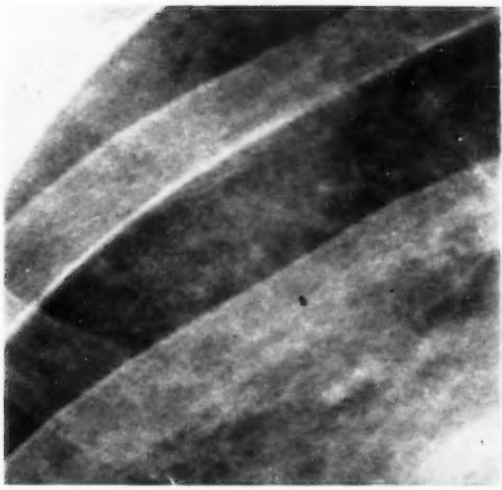

FIG. R. The right mid zone from a chest radiograph of coalminer with simple pneumoconiosis. The typical minut opacities are evenly distributed

FIG. S. The right mid zone from the chest radiograph illustrated in fig. T. Minute opacities are aggregated into clumps giving an appearance of " granular nodulation "

FIG. T

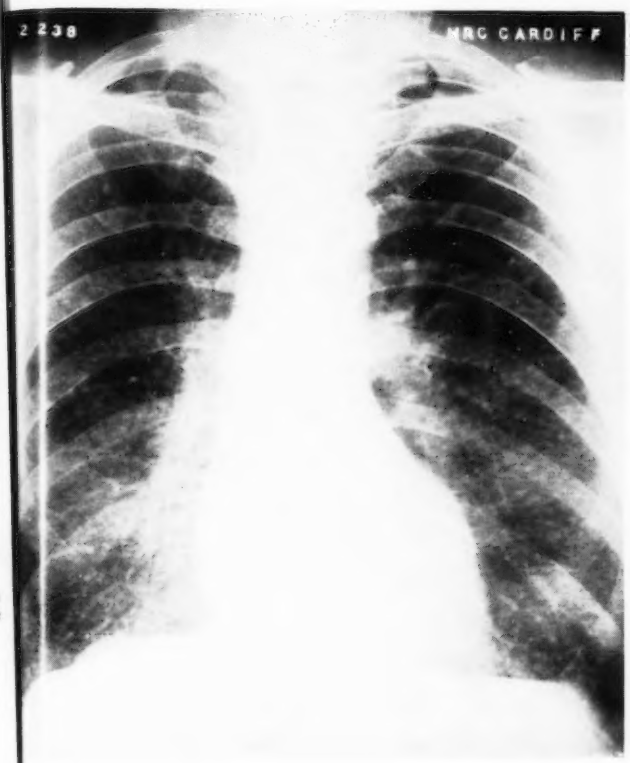

FIG. T. A typical example of simple pneumoconiosis (category 3) in a South Wales coalminer. Opacities of various sizes are distributed throughout both lung fields but are less profuse at the apices. Enlargement of the opacities (fig. S) shows that they have a granular appearance

FIG. U. Chest radiograph of a man aged 38 who had worked for 23 years in a semi-bituminous coalmine. In both upper and mid zones there are extensive coalescing nodules of a more homogeneous consistency than those typical of simple pneumoconiosis. These are characteristic in distribution and appearance of a relatively early stage of progressive massive fibrosis (category A). The man had very slight disability. Sputum was negative

FIG. W. Chest radiograph of the same case as fig. U taken 11 years later. He had not been exposed to coal dust inhalation in the interval. The progressive massive fibrosis has now advanced, and massive shadows are present in both lung fields with emphysema at apices and base. The simple pneumoconiosis is obscured. Gross disability was present. On culture the sputum was positive for tuberculosis

FIG. U

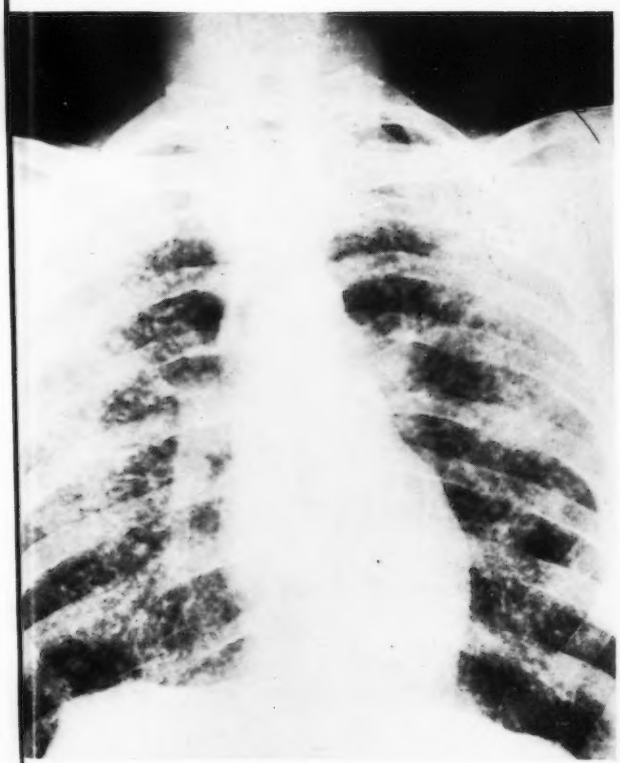

FIG. W

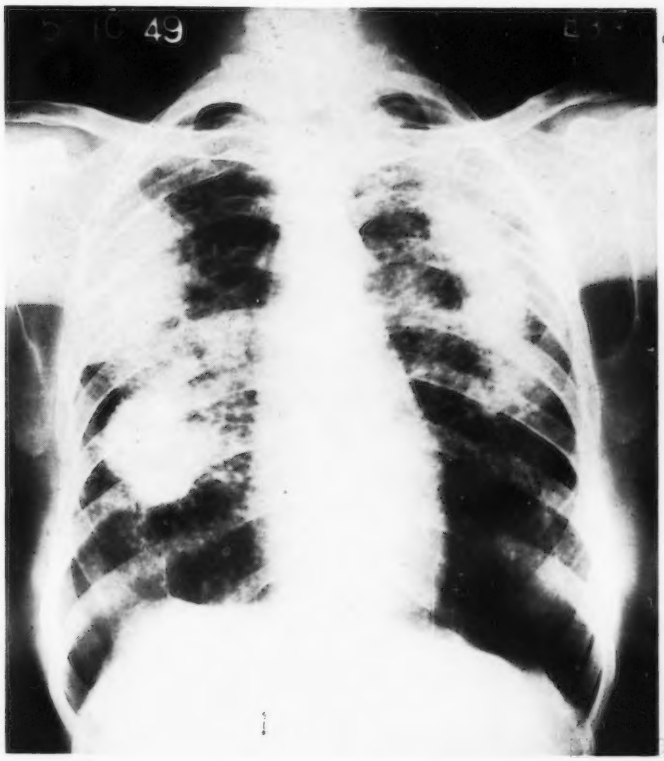

PLATE VIII (FIGS. Y, Z)

FULLERS' EARTH PNEUMOCONIOSIS
(FIGS. Y, Z)

E. L. Middleton
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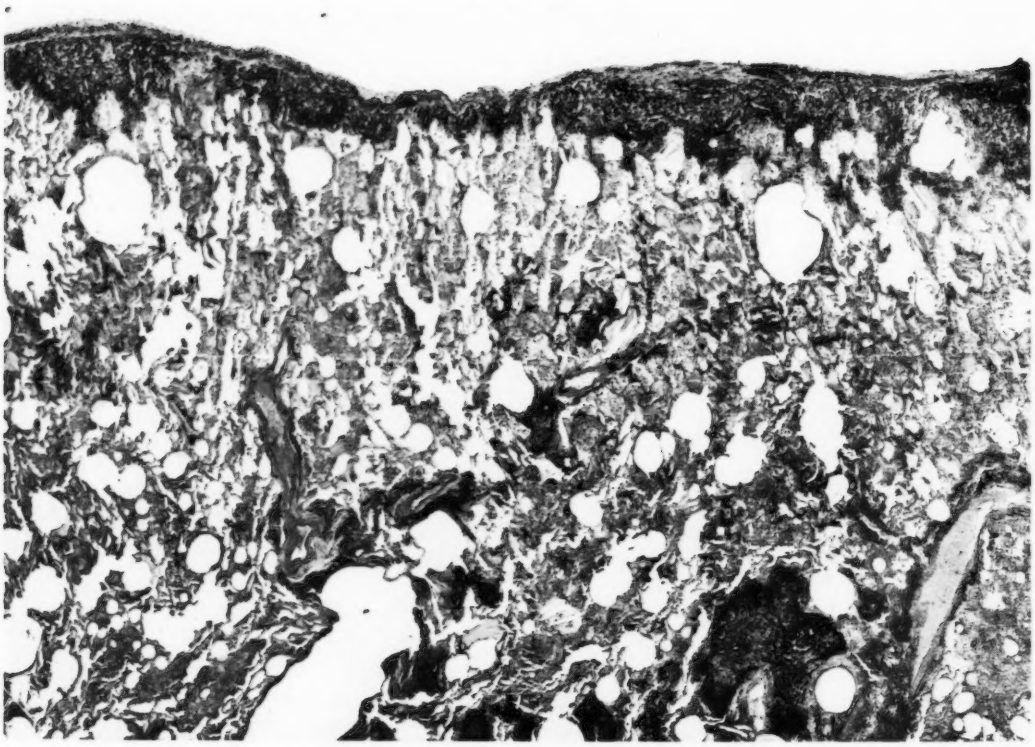

FIG. Y. Section of the lung and pleura ; showing fibrosis and air-containing tissue with numerous dilated air sacs (magnification × 16)

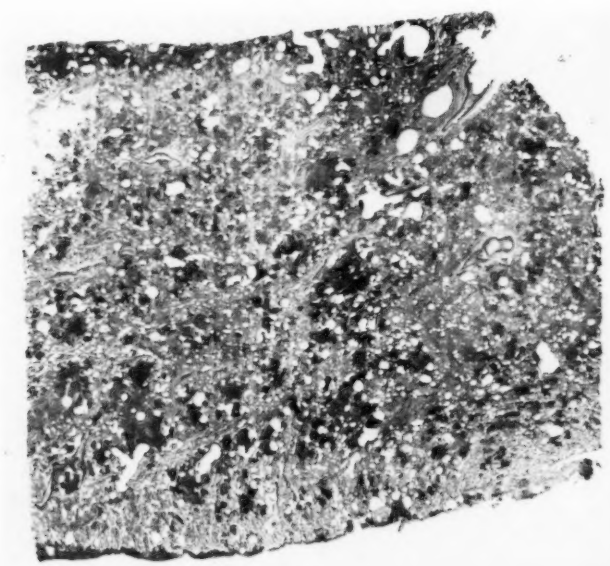

FIG. Z. Section of lung including pleura ; showing the general distribution of the fibrosis and the heavy impregnation with dust. By chemical analyses of portions of the lung Professor E. J. King found an average of 6.1 per cent silica and 3.6 per cent alumina in the dried lung tissue (magnification × 2)

4. Disability

The radiological and pathological investigations which we have described have thrown light on the nature and course of the disease, but have told us nothing about the important question of disability. Disability from pneumoconiosis takes the form of abnormal shortness of breath on exertion; although cough and pain in the chest are common symptoms they are seldom seriously disabling. Hart & Aslett (1942) showed that " reticulation " (the approximate equivalent of simple pneumoconiosis) was not significantly disabling in young men but caused moderate disability in older men. Cases with " consolidation " (the approximate equivalent of complicated pneumoconiosis) were disabled in both age-groups but more especially in the elder.

Physiological studies of disability recently made by the Pneumoconiosis Research Unit confirm these findings (Gilson & Hugh-Jones, unpublished observations). For instance, using reduction of maximal breathing capacity as an index of breathlessness, it was found that normal men, without any history of exposure to dust inhalation, showed a gradual diminution in this index with advancing age. Cases of simple pneumoconiosis of whatever category showed in each age-group a slightly lower maximum breathing capacity, which, in men aged 55 and over, was sufficient to indicate moderate disability. In each age-group, cases with complicated pneumoconiosis, especially in its more advanced stages, showed a serious diminution in maximum breathing capacity; in men aged 55 it was only 25% of that found in normal men of the same age.

We may therefore conclude that serious disability in coalminers' pneumoconiosis is caused chiefly by the development of complicated pneumoconiosis, although simple pneumoconiosis may also cause a moderate degree of disability. It must, however, be recognized that there are exceptions to this general rule. We do occasionally find men with simple pneumoconiosis who are seriously disabled, but in such cases it is difficult to exclude the possibility that emphysema, not of industrial origin, is contributing to the disability; we also find a few men with extensive massive fibrosis in whom the disability is unexpectedly slight.

5. Prevention

Any system of preventing pneumoconiosis must try to prevent men becoming disabled by the disease. Complete prevention can only be achieved by the effective suppression of dust in the men's working places. This is an engineering problem and, although great strides have been made in the South Wales coalfield towards the reduction of dust concentrations underground, we cannot yet say that the concentrations have been reduced to a level at which pneumoconiosis will be entirely prevented. We therefore need some additional means of prevention.

Fletcher (in press) suggests that this could be achieved by the institution of periodical *x*-ray examinations of all underground workers. If, as the result of such examinations, young men who show simple pneumoconiosis approaching the upper limit of category 2 were advised to cease working under conditions of dust exposure, their pneumoconiosis, according to his findings, should not progress any further. Moreover, since progressive massive fibrosis is seldom found radiologically except on a background of simple pneumoconiosis of at least the third category, such men should rarely develop complicated pneumoconiosis with its consequent serious disability. Men who are found to have already developed simple pneumoconiosis of the the third or fourth category, or cases with early complicated pneumoconiosis, could be advised to remain at their work under supervision; for there is evidence that further dust exposure has no effect on the liability of men to develop P.M.F. or on the liability of this condition to progress.

If dust concentrations in the mines are to be reduced to levels at which pneumoconiosis will not arise, it is essential that we should know more about the relationship between dust concentration and disease incidence, and to know whether there is a simple quantitative relationship between these two or whether the nature as well as the quantity of the dust which a man inhales determines his liability to develop pneumoconiosis.

We have already referred to Hart & Aslett's suggestion that there is a relationship between the rank of coal and the incidence of pneumoconiosis (Hart & Aslett, 1942). In South Wales, however, where their studies were carried out, there is a rough relationship between rank of coal and dust concentration in the mines, the anthracite mines being in general dustier than those of lower rank. Thus the varying incidence of the disease in South Wales might be explained as easily by a simple quantitative relationship between dust concentration and disease incidence as by a more complicated relationship which would include the rank of coal (Fletcher, 1948). We have also referred to the remarkable difference in the prevalence of pneumoconiosis between South Wales and the rest of Great Britain. It is, in general, true that the mines in South Wales are dustier than those in the rest of Great Britain. However, two mines in England where the dust concentrations are as high as any that are found in South Wales have recently been investigated by the Pneumoconiosis Research Unit. Underground workers at these mines have been *x*-rayed and it has been shown that the incidence of pneumoconiosis is very much lower than at Welsh mines where similar dust concentrations have existed for at least ten years (Cochrane, unpublished observations).

This most important observation shows that there is no simple quantitative relationship between the concentration of dust to which men are exposed and their liability to develop pneumoconiosis. The dusty mines in England, which had the low incidence of pneumoconiosis, were mining a very low-rank coal; this fact lends some support to the "rank-of-coal" hypothesis advanced by Hart & Aslett (1942). Chemical analysis of the dust at these different mines has not suggested that the silica content of the dust decides the incidence of disease in men exposed to it. This does not mean that silica may not be concerned, for Hart & Aslett showed that men working in rock and exposed to high concentrations of silica were much more prone to develop silicosis than men exposed only to coal dust. It must, however, be emphasized that although pneumoconiosis of coalminers is widely held to be a modified form of silicosis, the disease is very different pathologically from classical silicosis. Our evidence only suggests that the incidence of coalminers' pneumoconiosis itself bears little relation to the silica content of the inhaled dust.

Further studies are being planned to throw light on the relationship between disease incidence and dust exposure. Mines at which dust concentrations have for many years been low will be investigated in order to establish more precisely the maximum dust concentration in coalmines of

different types to which men may be exposed with impunity during their working life.

6. Treatment

There are two main methods of treatment. In the earlier cases, with only mild disability, much can be achieved by reassurance and a course of rehabilitation, with general exercises aimed at improving the general health of the men, and with special breathing exercises designed to ensure the best use of their lungs. In later cases, bronchial spasm plays an important part in the disability, and we find that often this may be effectively treated by the use of anti-spasmodics, particularly by the inhalation of aerosols of adrenaline or neo-epenine (*iso*propylnoradrenaline). The prompt treatment of complicating respiratory infections by chemotherapy with sulphonamides and penicillin is also of considerable importance.

Since disability in pneumoconiosis is chiefly due to shortness of breath on exertion, men affected by it cannot undertake jobs which entail heavy manual labour. Apart from this, they are capable of a wide variety of employment and many men can and should continue to work in the mining industry. The finding of a suitable job for a man partially disabled by pneumoconiosis is one of the most important aspects of his treatment, for depression due to unemployment appears to result in physical as well as mental deterioration. The question of employment of men with coalminers' pneumoconiosis in South Wales is reviewed by Hugh-Jones & Fletcher (in press).

7. Summary

The widespread disease of anthracosilicosis of coalminers is now known to be due to the inhalation of coal dust. The disease is pathologically distinct from silicosis and is better called pneumoconiosis of coalminers or coalworkers. There is a "simple" pneumoconiosis due merely to deposits of dust in the lung with minimal fibrosis but with focal emphysema often surrounding the dust foci, and a "complicated" or "infective" pneumoconiosis in which added infection (almost certainly tuberculous) leads to the formation of massive fibrosis. The two processes can be distinguished radiologically. Development and progression of simple pneumoconiosis is related to dust exposure, but the development and progression of massive fibrosis occurs independently of dust exposure after a certain critical degree of simple pneumoconiosis has been established.

Disability in simple pneumoconiosis is seldom severe except in older men. Massive fibrosis is a common cause of severe disability and death.

Coal dusts from different mines vary in their tendency to produce simple pneumoconiosis. Their pathogenicity does not appear to be directly related to their free silica content, but may depend upon some property associated with the "rank" of the coal.

Rehabilitation and treatment consists chiefly of general and breathing exercises, and using antispasmodics for cases with bronchial spasm. The provision of suitable employment is important.

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SILICOSIS AND OTHER PNEUMOCONIOSES

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1 Silica
a Etiology and pathogenesis of silicosis
b Diagnosis
c Prognosis and treatment
2 Mixed dusts or minerals containing free silica in significant proportion
a Granite
b Earthenware
c Graphite
3 Asbestos and other fibrous silicate minerals
4 Non-fibrous silicate minerals
5 Inorganic dusts without free or combined silica
6 Vegetable dusts
References

To the industrial hygienist the most appropriate definition of pneumoconiosis is that given in the Oxford English Dictionary (1933) as " disease of the lungs produced by inhalation of dust ; " this connotes symptoms and loss of function. It is well to keep in mind that the term has been applied to other concepts. Pathological changes in the lungs, with no occupational exposure to dust and no symptoms or loss of function, have been described by Policard (1947), Belt, Irwin & King (1936), Davson & Susman (1937), and Davson (1939), in what Stewart (1947) has called subclinical silicosis. Gardner (1936, 1940) considered the term pneumoconiosis too broad to be of practical use. For certain British legislation it has been defined as fibrosis of the lungs due to dust (National Insurance Industrial Injuries Act, 1946).

A convenient classification of the pneumoconioses is one based on the causative agents ; this fits in with the etiology and pathogenesis of the disease. Six classes may be recognized :

i. Silica as quartz, flint, chert, quartzite, and any highly quartzose material, including the forms cristobalite, tridymite and amorphous silica.
ii. Mixed dusts or minerals containing free silica in significant proportion.
iii. Asbestos and other fibrous silicate minerals.
iv. Non-fibrous silicate minerals.
v. Inorganic dusts without free or combined silica.
vi. Vegetable dusts.

1. Silica

a. Etiology and Pathogenesis of Silicosis

This disease is caused by the inhalation of uncombined silica, in particles which can reach the alveoli and remain in the lung in sufficient amount and over a certain period of time (Landahl & Herrmann, 1948). Fresh fracture has been suggested as a cause of rapid action ; Beyersdorfer (1948) has explained the effect on the crystalline structure of quartz of a shattering force liberating many tetrahedra with a free valency and greater chemical activity. But typical silicosis has been caused in man and in experiments on animals by quartz and flint long after they have been ground. The occurrence of rapidly developing silicosis was described by Macdonald, Piggott & Gilder (1930) in workers manufacturing and packing domestic cleansing powder who were exposed to the dust of quartzite long after it was ground. Of the 14 fatal cases in this series, followed up by Middleton (1936), one developed massive silicosis of the lungs and thoracic and abdominal glands, and silicosis of the spleen ; this spleen was examined and described by Belt (1939). Silicosis developing rapidly in the manufacture and packing of a cleansing powder containing 96% silica and 4% oxalic acid was described by Šrůter (1948) who considered that the oxalic acid had the accelerating effect. Rapidly developing silicosis has resulted from exposure to high concentrations of dust in tunnelling with pneumatic drills ; one such case was described by Charles *et al.* (1948) in a man employed for about 15 months on drilling ; he developed symptoms 44 months after leaving the dusty work. Similar cases have been reported by Lang & Zollinger (1949) among workers excavating rock galleries in Switzerland ; and cases have been reported in Sydney, New York, Johannesburg, and England in connexion with civil engineering work ; means for dust suppression were inadequate or entirely lacking. These might be regarded as instances of the effects of fresh fracture. On the other hand the chronic form of silicosis is found in sandstone masons who are exposed to particles freshly cut by the chisel ; here lower concentrations are important.

A different type of rapidly developing silicosis following exposure to calcined diatomite has been described by Vigliani & Mottura (1948). They describe the lungs in a fatal case as follows : solidified but without nodules ; thickened alveolar walls and obliterated air spaces. The calcined diatomite gave an *x*-ray diffraction pattern of cristobalite and the raw material did not. Vorwald *et al.* (1949) also found that flux-calcined diatomaceous earth showed a strong cristobalite pattern which was very faint in the raw material ; these authors found experimentally that both natural and flux-calcined material caused inflammatory tissue response, and that the diatomite component of the dust was less irritant than the cristobalite component formed in the calcining process. Shaver & Riddell (1947) described a series of cases of pulmonary disease resulting from exposure to fumes from electric furnaces in which bauxite, iron, and coke were treated in the manufacture of aluminous abrasives ; spontaneous bilateral pneumothorax was an early occurrence. In seven fatal cases autopsy showed an interstitial type of fibrosis of the lung with hyalinization, but there were no nodules except in one man who had previously worked underground as a miner. Jephcott (1948) described the fume from the furnaces as consisting of spherical particles from one micron down to a few hundredths of a micron in diameter. Analysis of the fume showed 29–44% silica ; the lung ash contained 0·86–2·45% silica and 1·16–2·57% alumina. The precise cause of this disease has not been definitely determined.

The size of particles causing silicosis has been regarded generally as being in the size range 5·0–0·5 μ ; or 1–3 μ

according to Sayers & Jones (1938); but, in fact, an agreed lower limit of size has not been fixed. Hatch & Kindsvatter (1947) showed that quartz particles with a calculated average diameter of 0·36 μ are retained in the alveoli and cause changes in the lungs, bronchial glands and spleen.

The amount of dust required to produce silicosis depends on the proportion of free silica present and varies, therefore, with the conditions. Irvine (1940) stated that in the gold mines of the Rand during the last ten years there was only 1 mg. of dust per cubic metre of air, and a certain amount of silicosis was still produced. Another estimate was made by Gessner, de Quervain & Bühler (1947). Particle size in relation to mass is important.

The relationship between duration of employment and the development of silicosis in certain industries is shown in the following table, which gives the fatal cases of silicosis, excluding those with manifest tuberculosis, reported to the British Factory Department up to the end of 1947:

TABLE I. FATAL CASES OF SILICOSIS WITHOUT GROSS EVIDENCE OF TUBERCULOSIS

Industry	Number of deaths	Duration of employment in years		
		Longest	Shortest	Average
Pottery	505	62·0	2·8	39·0
Sandstone	200	60·0	9·0	39·4
Grinding of Metals ...	91	56·0	14·0	36·3
Sandblasting	57	28·0	1·7	12·0
Scouring powders	12	37·0	2·3	8·4
Miscellaneous	172	57·0	1·5	22·9
Total Silicosis	1037	62·0	1·5	34·3
Total Silicosis with Tuberculosis ...	1046	67·0	0·7	31·3

The effect of tuberculosis is indicated by the figures at the foot of the table. In many very chronic cases of silicosis extensive spread of tuberculosis is a terminal event which does not greatly shorten life.

b. Diagnosis

Diagnosis is based on a complete occupational history, clinical examination, and a technically satisfactory radiograph. The clinical examination is directed principally to differential diagnosis, to discovering concomitant infections, and to determining the respiratory efficiency. Much research has been devoted to methods for the assessment of respiratory function; in Britain, pneumoconiosis especially of coal-miners has been studied. A study of the literature on the subject was made by Rossier, Bucher & Wiesinger (1947) who pointed out, as other observers have done, that the anatomical change does not always correspond with the loss of function.

Radiological examination, by flat film, stereoscopy and tomography, has taken a decisive place in diagnosis, and this is true for all forms of pneumoconiosis. Efforts are being made in Britain to standardize radiographic technique, and to relate appearances to known pathological lesions. Serial radiographs are often of value in diagnosis. Vigliani (1949) has described the extensive use of mass miniature radiography as a means of preventing silicosis and tuberculosis. This is now required by law in Italy, in certain industries, and Vigliani advocates the use of a mobile unit for speed and economy of work and materials. Delorenzi (1949) has also found the advantages of mass miniature radiography and suggests the setting up of a national centre, equipped with mobile units and with consulting experts. Outhred (1949) has described the use of a mobile unit, working in connexion with such a centre, in scattered gold-fields in Western Australia.

c. Prognosis and Treatment

Greinacher-Cristofari & Lang (1947) showed, from Swiss records, that removal of silicotics from dusty work at the earliest signs of the disease gives them an increased chance of avoiding serious disablement. Uncomplicated silicosis may remain stationary for some years (Outhred, 1949), but after a certain stage has been reached, progression of the fibrosis, with cardiac involvement or tuberculous infection, is liable to occur. Experience has varied in different industrial environments.

Denny, Robson & Irwin (1937, 1939) prevented the development of silicosis in rabbits by giving aluminium. Following the publication of their observations, treatment was undertaken of miners under 55, who had uncomplicated silicosis, and who continued to work in the mines. The results were reported by Crombie, Blaisdell & MacPherson (1944) to show subjective and functional improvement in some of the patients, while in others the condition remained stationary. Since that time much diversity of opinion has been expressed, approving or discrediting the treatment, and a considerable literature has been built up. Tabershaw & Tebbens (1945) have indicated the scope of such treatment and its contra-indications; these are chiefly tuberculosis and cardiac disease. Observations and experiments are still being continued and a final decision on the efficacy of aluminium therapy has not yet been reached (*Journal of the American Medical Association*, 1946). A controlled study of aluminium therapy in a limited number of advanced silicotics was made by Berry (1948), but he reached no definite conclusions. Patients with chronic silicosis and tuberculosis are not good subjects for sanatorium treatment, but physical therapy may prove beneficial for non-tuberculous cases of pneumoconiosis, as has been shown by Perret & Mattei (1949) at a special institution for miners in France. There, within the restricted means at present available, tests of respiratory function are applied and radioscopic examination of the chest is made. Patients are classified on the results of these examinations, and treatment is prescribed; this includes physical culture, controlled team games, and graduated work in the open air; medical treatment includes respiratory re-education, the administration of aerosols for bronchial spasm, and de-sensitization by intravenous injection of various drugs.

2. Mixed Dusts or Minerals Containing Free Silica in Significant Proportion

It has been estimated that silica, 12% of which is in the form of quartz, constitutes 59% of the earth's crust (Geological Survey, 1918). As one consequence of such ubiquity, minerals are often associated with quartz, and in the extraction, manipulation and use of such natural products quartz may be present in the dust in varying proportion; thus many

igneous rocks, such as granites, contain crystalline quartz; it is present in slate, in and between the laminae; haematite iron ore contains quartz, recrystallized from solutions which have infiltrated the iron deposits; and some minerals such as graphite contain only small proportions as an impurity. Free silica is used in technology and the arts by artificial admixture, like flint in earthenware. Where dust is produced from any such mixtures, natural or artificial, and inhaled, the essential action is that of free silica; it is in fact silicosis, but it is modified by the other constituents which may act as adjuvants, or may inhibit or buffer the intimate surface contact which is the condition necessary for the fibrogenic action of free silica. The degree of resemblance to typical silicosis is related to the percentage of free silica in the inhaled dust and to the influence of the other constituents; although, as Gardner & Redlin (1942) have shown, the amount of free silica found in the lungs does not necessarily correspond with the severity of the reaction or with the duration of employment. Certain international standards have been suggested as guides for the preventive control of dust, though these concentrations are not necessarily safe for workers. They are based on the percentage of free silica as follows: above 50%, 5 million particles per cubic foot of air (175 per cm.^{3}); 5–50% free silica, 20 millions per cubic foot (700 per cm.^{3}); below 5% free silica, 50 millions per cubic foot (1,750 per cm.^{3}) (Department of National Health and Welfare, Canada, 1949).

A brief reference may be made to three representative industries out of many involving exposure to such mixed dusts; the examples to be considered here are granite, earthenware and graphite.

a. Granite

Confusion has sometimes arisen regarding the effects of granite dust because of the inclusion in the term granite of a range of igneous rocks of crystalline structure from the "acid" rocks, or so-called true granites, with a quartz content of about 10–35%, to the more basic granitic rocks containing little or no quartz. The extensive investigations made by the United States Public Health Service (1929) in Vermont, and by the Massachusetts Special Industrial Disease Commission (1934) referred to granite containing about 35% of quartz; the investigators were able to base the degree of danger on the atmospheric concentration of the dust and the duration of exposure; and a maximum allowable concentration was reached on a statistical basis of evidence of silicosis in different classes of workers. Sutherland, Bryson & Keatinge (1930), investigating the effects of British granites, found a consistently lower incidence of silicosis than in a comparable series among workers in sandstone, which may contain 50–90% of quartz (Sutherland & Bryson, 1929). Lochtkemper & Teleky (1932) found only the slightest evidence of pneumoconiosis among workers in a quartz-free basalt; a similar contrast in lung changes was found by Gutzeit (1934) in granite and a quartz-schist with a silica content of over 90%.

b. Earthenware

Earthenware contains plastic clays, silicate minerals, and free silica in the form of calcined flint. Processes in the manufacture of pottery from this material give rise to dust when particles are allowed to dry on benches, floors or overalls; the result is silicosis, with the slight radiological and pathological modifications characteristic of the disease in workers of earthenware pottery. The mortality rate from silicosis is high, 4·17–6·78 per 1,000 employed; but it is not so high as was that of pottery workers who were exposed to the dust of ground flint alone in the "placing" of unfired china ware in that material; this rate was 8·66 per 1,000 (Middleton, 1936). This process has been entirely abolished by the Pottery Regulations (1947), and alumina is generally used as the placing material as a substitute for flint.

c. Graphite

This mineral occurs in various parts of the world, always in association with quartz. Harding & Oliver (1949) found that samples from Ceylon, S.W. Africa and Korea contained 3·6–10% free silica; Parmeggiani (1949) states that in Italian graphite from Pinerolo free silica is about 11%. The clinical, radiological and pathological findings in workers exposed to dust of graphite have been described by Dunner (1945), Dassanayake (1948), Gloyne, Marshall & Hoyle (1949), Dunner & Bagnall (1949) and Harding & Oliver (1949). The radiological evidence of pulmonary changes often preceded subjective symptoms, and occurred after 10 to 15 years or more; it included scattered nodular shadows, and rounded conglomerate masses which varied in shape and size and, in some cases, were seen to contain cavities; their presence was confirmed by autopsy. The clinical picture was that of a slowly developing silicosis, whereas the radiological and pathological findings more closely resembled those of pneumoconiosis of coalminers; copious black graphite-containing liquid was found in the lungs, with numbers of "graphite bodies" resembling asbestosis bodies in general form (Gloyne *et al.* 1949). The large amount of carbon probably acted by upsetting the expulsive power of the lungs and thus allowed the quartz to exert prolonged localized action.

3. Asbestos and Other Fibrous Silicate Minerals

In the opinion of Stewart (1947) asbestosis is a more serious disease than silicosis. It is now recognized that the fibrous form of asbestos determines many of the characteristics of the disease: the particles, which may reach 100 μ in length, are caught in the bronchi and bronchioles; phagocytosis is imperfect; the bases of the lungs are chiefly involved; the essential lesion is diffuse, never nodular, fibrosis; "asbestosis bodies" are formed, presumably as part of a natural reparative process, and, when present in the sputum in clumps, are of diagnostic significance (Stewart, 1947).

Diagnosis is based on the following: a history of occupational exposure to asbestos dust; clinical evidence of increasing dyspnoea; physical signs of changes especially at the bases of the lungs; and radiographic evidence of diffuse veiling or ground-glass appearance, first at the bases and around the heart shadow (Merewether, 1933). Post mortem the lungs are enlarged and of tough fibrous texture; emphysema is often bullous at margins and apices, and the less fibrous parts may be the seat of congestive or inflammatory changes. Histological examination shows generalized fibrosis, thickened alveolar walls, and numerous asbestosis bodies. The association of asbestosis with cancer has suggested a causal relationship. A statistical analysis of the 31 cases of carcinoma in 235 cases of asbestosis reported to the British Factory Department in the 23 years 1924–46 is given in the Annual Report of the Chief Inspector of Factories (Ministry of Labour and National Service, 1949). The incidence of

carcinoma with asbestosis was 13·2%, compared with 1·32% with silicosis.

Talc dust was the cause of an interesting case of pneumoconiosis, occurring in a man who died from rheumatic endocarditis, and described by McLaughlin, Rogers & Dunham (1949). The talc found in the lungs consisted almost entirely of straight fibres ranging up to 10 μ in length, formed, perhaps, by a previously unsuspected second cleavage, parallel with the Z-direction; the non-fibrous particles apparently had been eliminated. This case illustrates, from a single material, the different reactions of the lungs to fibrous and non-fibrous silicate minerals. Bruusgaard & Skjelbred-Knudsen (1949) reported marked radiological changes in 9 out of 34 men employed in a talc mill in Norway for periods lasting from 7 to 24 years; there was less disablement than would have been expected from the *x*-ray appearances.

Sericite, another silicate mineral which forms acicular crystals, has been suggested as a cause of pulmonary disease by Mavrogordato (1926), Badham (1927), and Jones (1933). It occurs in many rocks in association with quartz, and has been found in the lungs of silicotics as a residual mineral; but, by itself, it has not been found to cause progressive fibrosis of the lungs, possibly because the fibrous particles are too small to have the effect caused by asbestos.

Sillimanite, one of a group of minerals which are silicates of aluminium, presents a fibrous crystalline form in the raw state and when calcined, but, unlike asbestos, the fibrous form is lost when it is crushed. Sillimanite dissociates at a temperature of 1,545° C. into mullite and a silica-rich liquid (Tilley, 1929). Gärtner (1947) suggested that this fact may be related to the histological changes, with the formation of small irregular nodules, found in a portion of lung of a furnace worker, and reported by Gärtner & van Marwyck (1947). In the examination of 16 workers exposed to dust of calcined sillimanite Henry & Middleton (1936) found radiographic changes, but no disability and no signs or symptoms which could be related to the dust exposure.

Glass Wool, a fibrous silicate but not a mineral, was the subject of experiments by Gardner (1942). He found that owing to the high electrostatic charge on the fibres it was impossible to maintain an appreciable concentration in the atmosphere and few fibres, 3 μ or less in diameter and 10–12 μ in length, penetrated to the alveoli. Unlike asbestos fibres, glass fibres are not retained in the respiratory bronchioles and they do not produce fibrosis. Gardner considered that this material lacks the basic physico-chemical properties required to produce fibrosis.

4. Non-Fibrous Silicate Minerals

In the absence of quartz and of fibrous structure, silicate minerals appear to produce radiographic changes accompanied by symptoms which are less severe than might be expected from the radiographic signs. The amount of change depends on the concentration of dust and the period of exposure. In a study among workers in mica, which may be taken as an example of non-fibrous silicate minerals, Dreessen *et al.* (1940) found pneumoconiosis in 8 men exposed to dust concentrations of from 18 to 50 million particles per cubic foot (640–1,760 per cm.^{3}) for periods lasting from 18 to 46 years.

Another non-fibrous silicate mineral with only a trace of quartz is fullers' earth, which contains 85–90% montmorillonite, a silicate of aluminium. Radiographic examination of five men exposed to the dust for periods from 4 to 39 years showed in three men, employed from 4 to 19 years, films within normal limits; two others, employed 35 and 39 years, respectively, had signs of fine punctate mottling and some coalescence. One of these men died, at age 56, after chest symptoms for some years and disablement for 18 months. An autopsy was made by Gloyne (Campbell & Gloyne, 1942) who described the condition found as soft patchy pneumoconiosis without massive fibrosis and with none of the hard nodular character associated with silicosis. From microscopic examination of a portion of one of the lungs Belt described "small black rubbery lesions, each of which appeared to represent the cut end of a small blood vessel or bronchus"; there was no silicotic nodulation or massive fibrosis, and no tuberculosis (Plate VIII, figs. Y, Z) (Middleton, 1940). The persistence of the pulmonary changes which follow impregnation by dust is shown in a case reported by Tonning (1949). This patient, when a young man, had been employed for about 15 years in the same fullers'-earth works as that in which the above cases occurred; he had gone to Canada and, after various employments, with no exposure to dust, died there at age 79 of pneumonia following an operation for cancer of the lip. The pathological changes found in the lungs resembled those found in Belt's English case (Middleton, 1940).

Two types of kaolin, from coal measures and china clay deposits, were tested by intratracheal insufflation in rats by King, Harrison & Nagelschmidt (1948). The kaolins produced only a very mild reticulin reaction in the lungs; a specimen of ignited kaolin, which contained amorphous silica in the form of a glass, produced slightly more reticulinosis but no fibrous silicosis.

5. Inorganic Dusts without Free or Combined Silica

The most important members of this group are the beryllium compounds. The toxicity of beryllium is discussed elsewhere in this number of the Bulletin,[1] but, since the inhalation of certain beryllium compounds can produce pulmonary lesions (acute pneumonitis, which is essentially inflammatory, and chronic granulomatosis, which is essentially proliferative), the pulmonary lesions must be regarded as within the definition of pneumoconiosis. It is of some interest to mention an analogy with silica; besides pulmonary lesions certain compounds of beryllium cause chronic cutaneous lesions when implanted in the tissues; similarly, a condition called pseudotuberculoma silicoticum has been described by Shattock (1917), and by Faulds (1935) who described two such cases, in which quartz-containing material was introduced into the skin and subcutaneous tissue by accidental injury.

Various other non-siliceous dusts have caused pulmonary lesions. Exposure to the inhalation of aluminium dust has given rise to a condition called aluminosis, or aluminium lung (Goralewski, 1939, 1940, 1941, 1943; Jäger & Jäger, 1941; Kahlau, 1941, 1942; Jötten & Eickhoff, 1942).

Nodular shadows were found by Smith & Perina (1948) in radiological surveys of workers exposed to silicon carbide and aluminium oxide. Bruusgaard (1949) found that 10 out of 32 workers, exposed exclusively to dust of silicon carbide, had definite radiographic changes in the lungs. It is possible only to mention here some of these causes of pneumoconiosis, and

[1] Hunter, p. 5.

it is clear that further observation and research are necessary where the inhalation of any dust is a contingent risk.

6. Vegetable Dusts

Sugar Cane. Bagassosis is the name given to a pulmonary disease due to the inhalation of dust from waste sugar cane after the sugar has been extracted and during its manufacture into fibre board. The first case in England was detected in 1940; the disease resembled a form of pneumonia, and the radiograph showed a generalized distribution of shadows which suggested an occupational origin. Further cases followed, and the condition has been reviewed by Perry (1947) who also described the conditions at the factory. Perry suggests that the vegetable dust may block the bronchioles and bring about an infective process. The disease has also been found in the USA where Schneiter, Reinhart & Caminita (1948), after examination of the material, found organisms resembling *Aerobacter cloacae*; they suggested that the toxigenic types of *Aerobacter cloacae* should be considered as possible etiological factors in the disease.

Tobacco. In a study of the tobacco drying and stemming industry McCormick, Smith & Marsh (1948) found that dust liberated in the processes contained from 22 to 58% of free silica, and that the particles were of respirable size. A maximum allowable concentration of 10 million particles per cubic foot of air (350 per cm.^{3}) was suggested.

Grain. Examination, by the writer, of atmospheric dust samples taken with Owens' Settlement Dust-Counter in the handling of grain in the holds of ships, showed that hairs and tips of broken hairs from the grain amounted to 190—3,880 in 500 cm.^{3} of air. These hairs and fragments ranged in length from under 0·1 mm. to over 1 mm. and were derived chiefly from the apical " brush " of wheat and rye, and from the paleae and awns of barley and oats; they were mixed with particles of other debris, mould spores and mineral matter. This dust causes irritation of the upper respiratory passages; Duke (1935) has ascribed to this cause cases of asthma among workers in flour mills in the USA. The reaction to this dust appears to be partly traumatic and partly allergic.

Besides these three examples, many forms of vegetable dust involve a risk of pulmonary disease which would be included among the pneumoconioses.

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BYSSINOSIS IN THE BRITISH COTTON TEXTILE INDUSTRY

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1 Natural history
2 Etiology
3 Incidence
4 Prevention and control
References

Respiratory affections were noted among workers in the British cotton industry more than 130 years ago. Jackson (1818) and Thackrah (1832) referred to " phthisical complaints ", " bronchitis " and " pulmonary maladies " among cotton operatives, but Greenhow (1860) was one of the first British observers to describe a cotton respiratory disease characterized by difficulty in breathing. He recorded that carding-room operatives were very apt to become asthmatic in middle life and few were long lived. This disease was later named card-room asthma or strippers' and grinders' asthma, as card-room workers—particularly strippers and grinders —were mainly affected. It is now called byssinosis, from βύσσος, meaning flax or cotton. It is officially recognized in Great Britain as an industrial disease. Workers who have been exposed to dust for an aggregate of 20 years, and who are disabled by this disease, are eligible for compensation under the provisions of the National Insurance (Industrial Injuries) Act, 1946. An extensive review of the literature by the United States Public Health Service (1947) reveals that a similar respiratory disease has been described in other countries, but it occurs mainly among the cotton operatives of Europe.

There have been several investigations of byssinosis, notably by Collis (1908), Middleton (1926), and Prausnitz (1936). Nevertheless its etiology is still obscure. Methods of dust suppression have been developed in the last 40 years, but the Department of Occupational Health, Manchester University, in their recent researches, have found a substantial number of Lancashire cotton operatives in the card- and blowing-rooms still suffering from the disease. It is, however, found only among those working in the dusty processes of preparing and cleaning cotton for spinning. Spinners and weavers are not affected.

1. Natural History

Byssinosis has three stages, which were defined in the *Report of the Departmental Committee on Dust in Cardrooms in the Cotton Industry* (Home Office, 1932). The first stage, that of irritation, usually occurs after the worker has been exposed to cotton dust for 5 to 10 years. He notices tightness of his chest when he returns to work after a short absence. Characteristically it affects him after the week-end break, hence it has been called the Monday Feeling or " Monday fever " (Prausnitz, 1936). The worker complains of dyspnoea, fatigue and sometimes cough. On the next day he has completely recovered. The symptoms are graphically illustrated in the words of a stripper and grinder, aged 44, exposed to cotton dust for 10 years :

> Monday is a different day to me. Getting to 11 o'clock I feel tight on the chest and short of wind, but I have no cough. Towards 5.30 I feel done and struggle for breath and I can't walk at my ordinary speed. I am a dead horse on Mondays but could fell a bull on Tuesdays.

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This condition may persist without progression until the worker leaves the industry. After he is freed from exposure to dust, all symptoms cease and there is no disability.

There has been some confusion by Gill (1947), and in the *British Medical Journal* (1948), of terms describing the early effects of exposure to cotton dust. Arlidge (1892) used the term " mill fever " to describe a condition affecting young flax operatives. They suffered from a truly febrile disorder with chills, nausea and vomiting, which disappeared after the first two to eight days in the mills. He observed a similar, but less severe, condition in young employees recently starting work in other textile factories. Collis (1915) confirmed its occurrence among young cotton operatives. " Mill fever " should not be confused with " Monday fever ", the first stage of byssinosis as described above.

The second stage of byssinosis is characterized by a gradual progression of symptoms. Tightness of the chest and the dyspnoea get worse and occur on days other than Mondays. The progression is well described by an operative 46 years of age :

> I first noticed Monday Feeling about 15 years ago, and at first I only got it on Monday, but now I get it every day and I don't think there is much difference between my condition on Monday and other days of the week. Now I am always short of breath on exertion.

In the second stage of the disease, as in the first, symptoms cease when there is no longer any exposure to dust. The Departmental Committee, in their report referred to above, termed it the stage of temporary disablement or incapacity, as it led to short intervals of incapacity.

Many of those who reach the second stage get progressively worse and pass into the third stage, that of disabling byssinosis. Tightness of chest and effort intolerance are present every day and are so severe that the worker may have to give up his job. When he leaves the industry he experiences some relief, or at least the progress of the disease is retarded, but effort intolerance remains as a permanent disability.

The Departmental Committee described the signs and symptoms of byssinosis as those of chronic bronchitis and emphysema as seen in the general population, but the clinical and occupational histories are sufficiently characteristic for a definite diagnosis to be made. Recent investigations have confirmed that emphysema is the essential lesion, and that bronchitis is not invariably present as a clinical entity, even in the third stage of the disease. Of 33 men with disabling byssinosis, O'Sullivan (personal communication) found that 12 had no clinical evidence of bronchitis. Unlike most industrial pulmonary diseases caused by dust, there are no characteristic *x*-ray changes. Dunn & Sheehan (1932) reported on ten autopsies of cotton mill workers. Nothing of a specific nature was discovered, but lesions of chronic bronchitis and emphysema were found in nine cases, of which six showed hypertrophy of the right ventricle of the heart, thus indicating the severity of the condition.

GLOSSARY OF UNFAMILIAR INDUSTRIAL TERMS

Blowing-room	a room in a cotton mill where the cotton fibres, after unpacking, are separated and cleaned by a machine
Card-room	a room where the cotton fibres are further separated and cleaned and at the same time are drawn out into parallel lines in the carding engines
Ring-room worker	one who is employed in the ring-spinning room and who is not exposed to fine cotton dust
Scutching	one of the processes in the cleaning of cotton
Stripper and Grinder	one who strips the dust and cotton fibre adhering to the wire teeth of the carding engine and who sharpens the teeth by means of revolving rollers covered with emery

2. Etiology

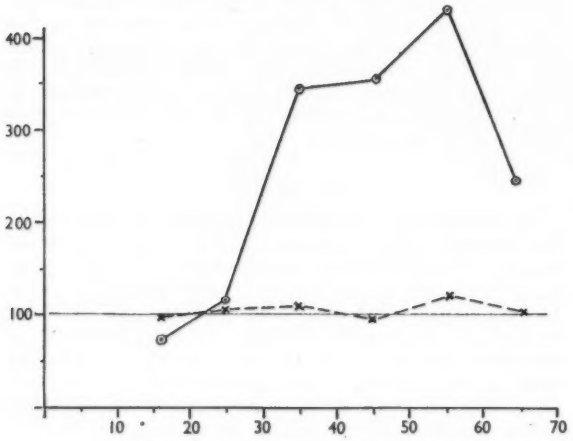
The etiology of byssinosis is still a subject for speculation. The causative agent is unknown and its mode of action is obscure. Prausnitz (1936) concluded from his experiments on man and animals that it is the protein fraction of cotton dust which is primarily toxic and is probably responsible for the changes occurring in the lung. His explanation of the pathogenesis of byssinosis was that the fine dust particles penetrate into the alveoli and eventually pass into the interstitial tissues of the lung, there exerting a chronic irritative action. The coarser fibres act on the mucous membrane of the upper respiratory tract, producing bronchitis, cough, and ultimately emphysema. Prausnitz demonstrated allergic supersensitiveness to the protein but considered that the substance resembling histamine in cotton dust played no important role in the disease. Haworth & Macdonald (1937) were less inclined to dismiss histamine as an unimportant etiological factor. They suggested that strippers' asthma might be caused by the combined action of a protein allergen and histamine. It seems a reasonable hypothesis that there is in cotton dust some protein allergen either of vegetable origin, or derived from micro-organisms or fungi which are known to grow freely in the cotton and to be widely distributed in the atmosphere of card-rooms. The allergen, after a time, sensitizes the bronchial mucous membrane and exposure to dust elicits bronchospasm and possibly swelling of the bronchial mucous membrane. This condition is reversible, but in workers with a high degree of sensitivity, and after prolonged exposure, the cough and spasm eventually give rise to emphysema, which is the cause of permanent disability.

Physicians with clinical experience of this disease have considered its etiology only in physical terms, that is to say, as the action of a toxin or allergen on the bronchial mucosa or the alveolar walls. But the asthmatic symptoms, with their characteristic periods of crudescence, intermission and recurrence, imply that the personality of the worker may play some part in etiology. There is as yet no evidence that byssinosis is a psychosomatic affection, but its natural history and symptomatology suggest a psychological as well as a physical approach to its investigation.

3. Incidence

In a recent investigation by the Department of Occupational Health at Manchester University 103 men over 35 years old with at least 10 years' exposure to dust in card- and blowing-rooms of mills spinning raw cotton of coarser grades were examined. Of these, 38 % had no symptoms, 52 % had symptoms of early byssinosis (first and second stages) and 10 % had reached the third stage of disabling byssinosis. Susceptibility appeared to bear no relation to other respiratory diseases. The incidence of byssinosis was

FIG. 1. SICKNESS RATES FOR COTTON STRIPPERS AND GRINDERS, 1923-27



After Bradford Hill, Industrial Health Research Board Report No. 59

Abscissae : age in years
Ordinates : sickness rates expressed as percentages of the sickness rates of male cotton ring-room and warehouse workers

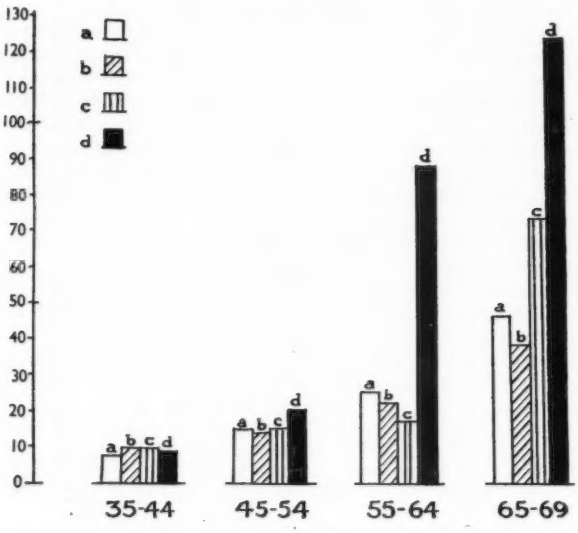
——— respiratory causes
- - - - - - - all causes excluding respiratory

significantly lower in another group of mills which had less dust in the atmosphere of the card-rooms. In these latter mills, among a similar group of 140 men, 70 % were free from symptoms, 25 % had reached the first and second stages and 5 % were disabled by byssinosis. Thus dust concentration and individual susceptibility are important factors in determining incidence ; and herein lies the key to the prevention of this disease.

Bradford Hill (1930) compared the sickness incidence of strippers and grinders with that of warehousemen and ring-room workers in the period 1923–27. When respiratory diseases were excluded there was little difference in the rates. But after the age of 30 the strippers' and grinders' sickness rates from respiratory disease were two to three times as high as those of warehousemen and ring-room workers, that is to say, of men working in the same industry but not in the dusty rooms (see fig. 1). Harvey (1939), who was a member of the Departmental Committee on Compensation for Card Room Workers, examined morbidity rates for a later period (1935–1936) to see if card-room workers still suffered excessively from respiratory disease in spite of the steady improvement in working conditions. He found that between the ages of 30 and 45 the sickness rates from respiratory causes for card-room workers were 181% of those of spinners and weavers.

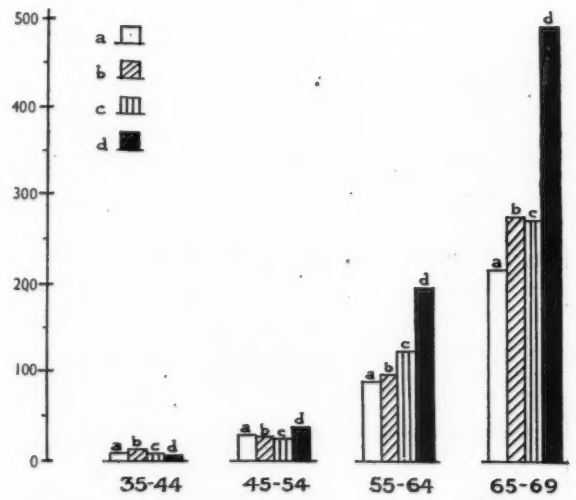
The most recent occupational mortality rates are given by the Registrar General (1938) for the triennium 1930–32. As for the previous triennia 1910–12 and 1921–23, these show excessive mortality from respiratory and cardiovascular diseases for strippers and grinders over the age of 55 (see figs. 2, 3) compared with other cotton operatives and all males over the same age. The reason for the high mortality from cardiovascular diseases is still obscure, but Schilling &

FIG. 2. DEATHS FROM RESPIRATORY DISEASES 1930–32



Abscissae : age in years
Ordinates : rates per ten thousand
a : all males
b : cotton weavers
c : cotton spinners
d : strippers and grinders

FIG. 3. DEATHS FROM CARDIOVASCULAR DISEASES 1930–32



Abscissae : age in years
Ordinates: rates per ten thousand
a : all males
b : cotton weavers
c : cotton spinners
d : strippers and grinders

FIG. 4. STRIPPING BRUSH FITTED WITH EXHAUST

Goodman (unpublished) have shown that a substantial proportion of cardiovascular deaths should be classified as respiratory deaths. Up to 1939 the Registrar General's rules for selecting one disease from certificates with more than one cause of death gave preference to any disease of the heart or kidneys over a respiratory disease. As the terminal stage of byssinosis may be one of congestive cardiac failure, heart or renal disease is likely to be mentioned on the death certificate, and thus selected by the Registrar General as the cause of death. It is evident, therefore, that mortality from byssinosis has been under-estimated in the past. The actual number of cotton operatives who are disabled by byssinosis represents but a fraction of the total population in the cotton textile industry, but those at risk are a vital link in the production chain. If the card-rooms are undermanned, owing to absence through sickness or because apprentices are discouraged in these days of full employment from starting a career which may lead to disability in middle life, the whole industry suffers. Thus this industrial disease has economic and social ill-effects which cannot be measured merely in terms of its incidence and the disability, discomfort and ill-health it causes among card- and blowing-room workers.

4. Prevention and Control

Since the second decade of the present century, much has been done to reduce the concentration of dust in card-rooms by fitting the stripping brush with an exhaust (see fig. 4), by vacuum cleaning and by removing dust from the atmosphere of card-rooms by air conditioning. These measures and others devised by the industry and the Shirley Institute of the Cotton Industry Research Association have reduced the incidence and severity of byssinosis. The Departmental Committee on Compensation for Card Room Workers (Home Office, 1939) were of the opinion that, although the results of the two investigations made respectively by Bradford Hill in 1930 and Harvey in 1939 were not exactly comparable, the disparity between the figures for 1923–27 and those for 1935–36 permit the conclusion that improved conditions of work had had markedly beneficial results. However, the results of investigations in 1948 and 1949, already quoted, reveal that the disease is found in more than 50 % of men over 35 with at least 10 years' exposure in mills spinning the coarser grades of cotton. Although the majority never become handicapped by the disease, a few men are disabled in the fifth and sixth decades of life.

Great interest has recently been aroused by new methods of applying oil emulsion to raw cotton in order to suppress dust. Twenty years ago oiling of raw cotton was given an extensive trial. It failed because it caused loss of strength in the yarn. The new methods described by Paton (1948) are now being adopted in more than one hundred Lancashire spinning mills. The oil is sprayed from a direct liquid pressure system through a nozzle in the hopper of the hopper feeder regulator (see figs. 5, 6), that is, before the cotton is scutched and carded. The Chief Inspector of Factories has reported that dust-counts in card-rooms of mills where oiling is installed "have shown that the reduction in

FIG. 5. SPRAY INSTALLATION ON HOPPER FEEDER REGULATOR

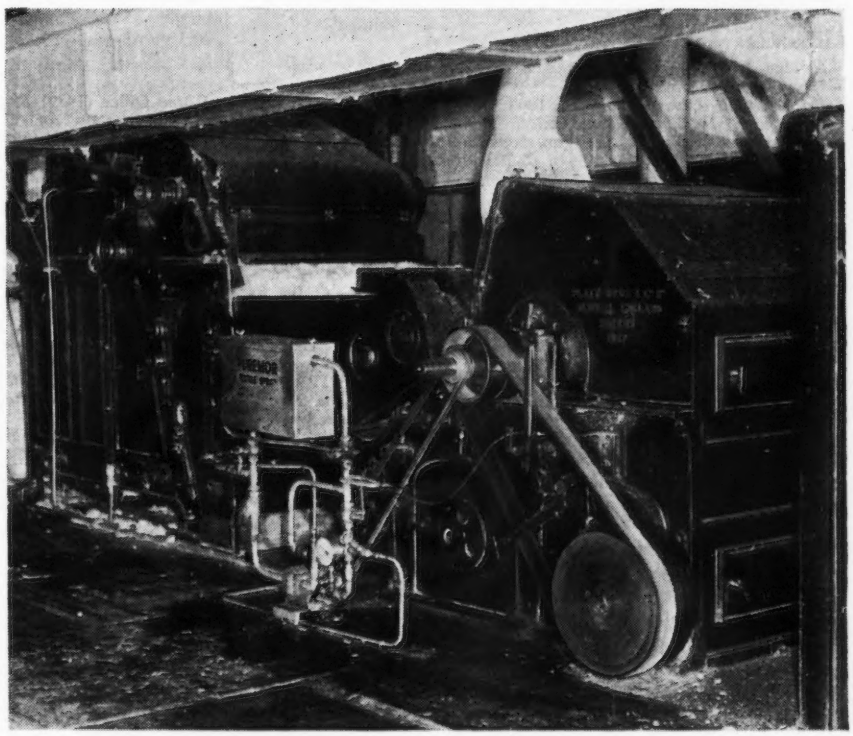
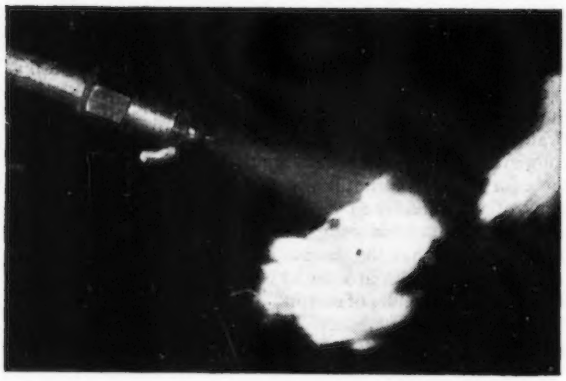


FIG. 6. OIL SPRAY INSIDE HOPPER



the visible fraction in card room air is in the region of 45 per cent., and in the invisible fraction, that is, the fraction most dangerous to health, about 55 per cent." (Ministry of Labour and National Service, 1949). In a recent investigation in 8 mills, 16 men out of 35 working in the card- and blowing-rooms were found to be complaining of tightness of their chests. Three months after oiling was introduced 8 of the 16 men lost their symptoms completely. It was not possible to eliminate the effect of psychological factors, as the men knew that oiling had been introduced and expected improvement, but to some extent an unexpected control of the psychological factor was provided by a mill which had technical difficulties with oiling shortly after its installation. Some of the card-room workers who noticed an improvement or a loss of symptoms in the first eight days complained thereafter that conditions were as bad as ever. They did not know that the oiling process was at fault, and suggested that the deterioration in conditions was due to the use of a lower grade of cotton. Twelve months after the first examination, the initial improvement noticed in the eight men mentioned above was not maintained. This suggests that the oiling process still needs to be improved technically, but there is reason to hope that a satisfactory method of further reducing the incidence and severity of byssinosis has been found.

It has already been shown that susceptibility is an important factor in etiology. The industrial medical officer has the opportunity of preventing disability from byssinosis by examining periodically men exposed to dust, and by encouraging those with signs of progression to change their jobs.

Although byssinosis is an industrial disease which can be prevented, this has not yet been done successfully. Much work is needed to clarify its etiology and to improve methods of dust suppression. Industrial medical services have been developed with some success in the more modern factories producing aircraft, motor-cars and chemicals. In the much older textile industry with its long established hazards of respiratory disease and mule spinners' cancer, there are few medical officers, and these must depend on their clinical experience to prevent disease among cotton operatives.

ACKNOWLEDGEMENTS

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OCCUPATIONAL RADIATION HAZARDS

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1 Occupations with potential radiation hazards
2 Known clinical results of occupational exposures
3 Evaluation of radiation hazards
4 Radiation dosage measurement
5 Maximal permissible exposures to radiation
6 The practice of radiation protection
  a Preliminary evaluation of the radiation hazards
  b Planning methods of operation
  c Training and supervision of operatives
  d Hazard detection and measurement
7 Health supervision
Select bibliography

The penetrant properties of ionizing radiations continue to prove of increasing applicability and value in industry, medicine, and many types of scientific research. There is consequently a progressive increase in the number of persons coming into regular occupational contact with radiating equipment and installations and with natural or artificially-prepared radioactive substances. The tendency also continues towards the use of more and more powerful radiating equipment and the handling or use of radioactive substances in greater concentrations or quantities than previously, since these increases usually enhance the value of radiation for special investigations or practical applications. It is impossible as yet to forecast the extent to which penetrating radiations will feature in the industrial, medical, research, and even everyday activities of future generations. The present indications are that scientific evolution and developments may result in an increasing number of persons being regularly exposed to radiation in excess of the natural background of their environment, either occupationally or in consequence of these trends towards increased general use. It is of recognized importance that increasing utilization of penetrating radiations should not be accompanied by increased risks to the health of those exposed.

Developments in the last decade have extended the province of occupational radiation hazards very significantly. This is particularly notable in the diversity of the sources of radiation now encountered in research establishments, development laboratories, hospitals, medical centres, in many established industries, and in recent industries connected with the utilization of nuclear energy on a large scale. This article is therefore intended only as a review of the present situation. It also summarizes the methods by which potential radiation hazards may be assessed and as far as possible brought into line with potential hazards occurring in other industries. As it is largely a synopsis, references are not included in the text, but a bibliography of related literature on special aspects of the subject is appended.

1. Occupations with Potential Radiation Hazards

Latent health hazards from penetrating radiations now exist for many diversely employed and diversely skilled groups of persons. The potential risks are, however, by no means always confined to those directly employed in such activities, since the penetrating properties of the long-range radiations frequently extend beyond the immediate working area, and the emission of radioactive gases, dusts, solutions, or other forms of contamination outside the immediate area of operation, may greatly increase the radius of possible health hazards. The occupations concerned may be divided into two groups as follows :

From radiating equipment

Medical *x* radiography
Medical *x* radiotherapy
Medical radium therapy

Industrial *x* radiography
Industrial gamma radiography

Physical research on nuclear energy
Direct utilization of nuclear energy
Preparation and distribution of gamma-radiating " sources '

From radioactive substances

Radioactive ore mining
Ore processing and refining

Production and distribution of artificial radioactive isotopes

Chemical research with radioactive elements

Industrial applications, e.g., luminous paint, thorium mantles, static eliminators

Isotope research, for such purposes as :
  i. medical, including therapy ;
  ii. industrial process control and investigation ;
  iii. biological, pharmacological and other fundamental or applied problems

Utilization of nuclear fissile materials for defence or power purposes.

2. Known Clinical Results of Occupational Exposures

In the past fifty years four main exposed groups have exhibited radiation injuries.

i. The first group includes the early workers with radioactive substances and *x* rays, mainly physicists, chemists, doctors and technicians engaged in pioneer research or medical therapy. In some cases dermatitis and finally malignant changes developed in the skin of the hands, and the incidence of leukaemia in some of the occupational groups was eventually well above the average level for the community.

ii. The second group includes the uranium ore miners of the Joachimstal district of Saxony, in whom the incidence rate of bronchial or mediastinal carcinoma was eventually demonstrated to be very high by comparison with that in a non-exposed community. Although it is true that these miners were concurrently exposed to non-radioactive dusts containing arsenic, cobalt and nickel, it is also true that there resulted a high degree of contamination of the mine atmosphere with radon gas and radioactive dusts from the uranium-radium content of the ore. Subsequent calculations have strongly suggested that these inhaled atmospheres would cause

irradiation of bronchial and lung cells to an extent well above what is now considered the threshold of injury.

iii. The third group comprises the several hundred persons engaged in the 1914–18 war on the painting of instrument dials with luminous paint, which contained about 1 part of radium or mesothorium in every 20,000 of zinc sulphide. There was at that time little evidence that the industrial methods, conditions and hygiene for this type of work were unsatisfactory, or needed to be of the high standard now expected. Probably in consequence, inhalation and ingestion of radium or mesothorium occurred in many workers, with deposition of the non-excreted fraction of the contaminant in the bones. The insidious nature of the eventual injuries, and the lengthy latent period usually associated with all but gross over-dosages, resulted in some delay before the true cause, " radium " poisoning, was assigned to the anaemias of aplastic type and the osteitis, necrosis and occasional osteogenic sarcomas of bone which occurred among these workers.

iv. The fourth group is a miscellaneous one. It includes, for example, research physicists who have recently exhibited posterior cortical cataract, presumably from relatively slight exposure to direct neutron beams ; technical and research workers whose exposures to radiation or radium are more or less known, and who have developed various degrees of leucopenia or other threshold changes ; cases of moderate to severe over-exposure in the early days of therapeutic radiation, or of accidental over-exposure during research or development work with highly radioactive materials.

The above four groups include, in all, many hundreds of minor or major radiation casualties. As has frequently happened in the study of occupational health, most of the investigations were made some years after the causative exposures, and it is likely that many further cases of radiation injury did in fact occur but were not traced. There has also been great difficulty in confirming the exact amount of exposure to radiation in these cases. Consequently there is, as yet, no clearly defined correlation between total radiation dose or dose-rate and the clinical sequelae to be expected, particularly at the lower levels of chronic exposures. For this reason—as with many other toxic agents for similar reasons—experimental animal exposures have been made on a large scale to try to fill in the gaps in existing human information.

The Present Situation

In the past decade a vast amount of biological experimentation has been carried out with radiations and radioactive substances upon many species of animals, particularly in laboratories in the USA, and the literature on the many very specialized facets of this problem has become voluminous.

The combined results of physical research upon the properties of radiations and radioactive substances, clinical observations on man, and exposures of animals under controlled conditions have provided a framework of information upon which an effective scheme of protection can be devised for any occupation involving radiation exposure. The degree of accuracy of much of the clinical and biological information is admittedly not high, but is probably high enough to meet the immediate needs of the situation. There is substantial agreement, for example, concerning three essential practical requirements :

i. The methods of preliminary evaluation and eventual confirmation of the occupational radiation hazards in a given set of circumstances.

ii. The types of clinical injury likely to follow harmful irradiation of the body tissues.

iii. The maximal permissible occupational exposures to radiation and radioactive substances considered to be reasonably safe in the light of present knowledge and experience.

3. Evaluation of Radiation Hazards

The physical properties of radiations and radioactive substances are sufficiently well known to allow preliminary physical calculations to be made of the radiation energy given out as *x*, gamma, alpha, beta or neutron radiation from any source, whether it be an *x*-ray installation, radon needle, industrial container holding radioactive ore, or a beaker of saline containing $^{24}NaCl$ for example. The precision of the calculated values may not be great, but generally serves for planning purposes, especially since the actual radiation energy flux and physical radiation intensity may be subsequently checked with reasonable accuracy by means of the radiation detecting and measuring devices available for the purpose. These devices include the now familiar Geiger tubes and ionization chambers connected to electronic counting, measuring and recording circuits. From available knowledge of the penetrant properties of the various radiations through air, water, or material of known density and composition, the calculated energy fluxes may be converted into an assessment of the radiation dosage at any point distant from the source. Such calculations made for planning purposes may later be checked by direct observation.

The ranges of penetration of the various radiations into air or any specified material vary not only with the density and chemical composition of the material but with the type of radiation and the total energy with which the radiation is produced at its source. An arbitrary division of the important radiations may be made by reference to their ranges of penetration, and is of immediate practical importance in evaluation and control of hazard.

i. *Long-range radiations* such as *x*, gamma, or neutron radiation, which may penetrate through several hundred metres of air, a few metres or many centimetres of water or body tissue, or a few centimetres or millimetres of dense materials such as lead, iron or steel before their energy has become fully dissipated in, and transferred to, the atoms of the absorbent medium.

ii. *Medium-range radiations* such as beta radiation, which may penetrate through several metres of air, one or two centimetres of water or body tissue, one or two millimetres of glass or aluminium, or less than a millimetre of lead, iron or steel before its energy is fully absorbed in the medium.

iii. *Short-range radiations* such as alpha radiation, which may penetrate through only one or two centimetres of air, or less than 50 microns of water or body tissue before its energy is fully absorbed. Alpha radiation is thus fully " stopped " by the interposition in its path of a thin layer of almost any everyday material.

The ranges quoted above are approximations only. A highly energetic or " hard " beta radiation may be as penetrant as a " soft " *x* or gamma radiation of very low energy, and alpha radiation of high energy may be almost as penetrant as " soft " beta radiation. From a knowledge of such factors, and by making the necessary allowance for the various degrees of " scattering " of *x* and gamma radiations from materials in their paths, a preliminary evaluation of the probable radiation hazard may be made, even when various types and thicknesses of operational materials are situated between the source and

the working positions. The evaluation can also be extended to the probable external radiation exposure arising from the presence in the working environment of a disseminated beta- or beta-gamma-emitting isotope as a gas, dust, fume or vapour.

The assessment of the probable effects of a certain physical dose or dose-rate of radiation on living tissue can be based only on study of the data obtained from close observation of humans exposed occupationally or, in some cases, therapeutically, and the data obtained from experimental animal exposures. The difficulty of such assessment is increased by the fact that animal exposures, if they are to simulate those occurring occupationally, must continue for most of the animals' life-span, correspondingly low dose-rates of radiation being required. These experiments are notoriously difficult to run, besides being difficult to interpret. As with all other toxic agents, the response of different species to radiation exposure varies considerably, and the extrapolation of animal data to human beings is correspondingly difficult. However, data do now exist for several species, permitting the assessment of the relationship of dose to mortality or of dose to effect, admittedly with insufficient accuracy to explain every finding, but with sufficient probability of truth to permit provisional safe occupational exposure levels to be defined. This now applies to most types of radiation, and to a fair proportion of radioactive elements. Where direct experimental evidence is not available for any particular radioactive isotope, knowledge of the metabolic fate of the element's stable isotope and of the physical properties of the active isotope permits an estimation to be made of the local tissue irradiation probable from absorption of the active isotope into the body via lungs, gut or other route, and selective deposition in the tissues. It has not been possible, however, to extend this method to all the isotopes capable of being produced during nuclear fission or by irradiation of materials in the nuclear reactor, since the information available on the metabolic pathways of many elements is inadequate for the purpose.

4. Radiation Dosage Measurement

The response of cells, tissues or the whole body to radiation depends, among other factors, upon the type, total dose and dose-rate of radiation concerned. Units of dosage and methods of measurement are therefore required. The customary unit of dosage for *x* and gamma radiation is the röntgen (r.), defined in effect as that amount of *x* or gamma radiation which, fully absorbed in 1 cm.^{3} of standard air, produces ions carrying one electrostatic unit (e.s.u.) of electricity. This proves approximately equivalent to the production of 2×10^{12} ion-pairs per gram of irradiated tissue, or 2 ion-pairs per cubic micron, or the absorption of 83 ergs energy per gram of tissue. Alpha and beta radiations are suitable for similar definition, and to cover all four radiations, the " röntgen-equivalent-physical " (rep) has been defined as that amount of *x*, gamma, alpha or beta radiation which, fully absorbed in 1 cm.^{3} of standard air, produces ions carrying 1 e.s.u. of electricity.

However, the dosage received by the tissues during occupational exposures cannot be measured directly, so that the total dose in r. or rep, or the dose-rate in r. or rep per unit time, must be measured at the surface of the body. Appropriate factors are then applied for the depth of penetration and energy absorption at different depths in tissue, varying with the type and energy of radiation. The surface dosage of *x*, gamma or beta radiation may be determined by the examination of photographic film worn on the clothing for known periods, or it may be estimated from the readings on radiation monitoring instruments calibrated in r. or rep/unit time. Some sense of the practical meaning of the rep may be obtained from such data as the following: the natural background gamma-radiation dose-rate at the earth's surface, due to cosmic radiation and that derived from radioactive materials in the earth's crust, approximates to 0.0001–0.0002 rep/day, or 3–5 rep/average lifetime. One millicurie (milligram) of radium, enclosed in a thin platinum shield to absorb alpha and beta radiation, causes a gamma-radiation dose-rate of 8.3 rep/hour at a distance of 1 cm., decreasing inversely as the square of the distance from the source. The average *x*-radiation dose to the exposed tissues during chest radiography is about 0.2 rep, while *x*-ray screening examinations may cause a dose-rate of 10–20 rep/minute to the exposed tissues. A single dose of from 400 to 800 rep of *x*-radiation is required to cause radiation erythema of exposed skin, while the available evidence indicates that the median lethal dose (LD_{50}) for *x* or gamma irradiation of the total body volume of man is about 450 rep. The maximal permissible *x*- or gamma-radiation dose-rate for occupational exposure is now recommended as not more than 0.5 rep/week measured at the surface of the body, i.e., 26 rep/year, or 520 rep/20 years. The prolonged and fractionated dosage in such cases is believed to give adequate scope for the recuperative powers of the tissues and cells, thus explaining the apparent anomaly of the LD_{50} dose being lower than the twenty-year accumulated permissible occupational dose.

Although it is true that very large radiation doses could be accumulated in a period of hours or days by exposure to large or powerful sources of radiation, the handling of radioactive sources and installations has been so well controlled since the 1920's that large radiation dosages are likely only as a result of abnormal occurrences or the wilful neglect of precautions. In the more severe types of occupational injury large total dosages or high dose-rates of radiation were involved; most of these cases date from the first thirty years' exploration and use of radioactivity. However, it must not be forgotten that the lengthy latent periods associated with most radiation injuries, especially just above the injury threshold, may yet result in further instances of occupational radiation injury becoming manifest, as a result of the rapid increase in the production and use of radioactive materials and the acceleration of research and development work on nuclear fission in the past decade.

Known Occupational Radiation Injuries

The main occupational radiation injuries known to date may be summarized as follows:

Skin. Acute dermatitis, with erythema, epilation, hyperpigmentation, ulceration, scarring, telangiectases, keloids, or hyperkeratosis.

Chronic dermatitis, with skin atrophy, nail-bed distortion, or indolent ulceration.

Malignant dermatitis as a possible sequel to the above forms, squamous or basal cell carcinomata developing on or away from the sites of previous known injury.

Blood. Granulopenia, lymphopenia, or their combination as leucopenia, possibly with presence of immature cell forms in the peripheral blood.

Hyperplasia, hypoplasia, and finally aplasia of the bone marrow, with consequent aplastic anaemia.

Leukaemia.

(It is generally agreed that the earliest detectable biological response to injurious levels of penetrating radiation of large volumes of the body is a change in the relative or absolute numbers of leucocytes in the peripheral blood. Because of the occasional finding of transient leucocytosis after irradiation, it has been thought that initial stimulation of the bone-marrow sometimes occurs, but the significant early change is invariably towards hypoplasia. In spite of the very large number of blood counts carried out in the past on radiation workers, there is as yet no precise evaluation of the relationship between the blood picture and radiation exposure.)

Lungs. Bronchial carcinoma, chiefly among the uranium ore miners in Saxony, with a few cases among radium chemists and dial painters.

(This effect is thought to follow not the occasional retention of inhaled scattered particles, but rather the chronic excessive irradiation of large volumes of bronchial or lung tissue, as after inhalation of radon and its decay to solid daughter-products, or from relatively heavy dosage with air-borne alpha-emitting materials.)

Eyes. Posterior cortical cataract has recently been reported in some nuclear research physicists exposed to neutron beams from cyclotrons. It may be assumed that these were in fact occupational injuries.

Bone. Osteitis, bone necrosis, and, in a few cases, osteogenic sarcoma of the long bones, jaw, spine and pelvis, occurring mainly among radium or mesothorium dial painters of the 1914–18 war. Similar effects have been noticed among radium chemists and persons taking radium ' therapeutically '.

The above list is confined to the most chronic occupational injuries and does not include all the observed biological sequelae of over-exposure to radiation, such as the acute radiation syndrome, radiation sickness, the effects on tissues of localized therapeutic radiation, or other effects producible in animal species by high over-dosages. The occupational hazards apparently latent in over-exposures to radiation or radio-active substances may be summarized as acute or chronic inflammation, with its sequelae; or degenerative changes including necrosis; or malignant developments in sensitive tissue, when subjected to sufficiently excessive over-dosage by ionizing radiation over a sufficiently lengthy period, the latent period being frequently much longer than in other occupational diseases.

5. Maximal Permissible Exposures to Radiation

The principle of the maximal allowable concentration as applied to other toxic agents in industry has been widely and carefully applied to radiations and radioactive substances. There is now fairly general agreement among workers in this field as to the maximal permissible occupational exposures to radiation or radioactive substances which may be allowed with reasonable expectation of safety. These values are similar to maximal allowable concentrations for other toxic agents as regards the reservations frequently necessary as to their degree of accuracy, the nature of the evidence on which they are often framed, the various factors of safety incorporated in them, and the method of their interpretation and application in practice.

Perhaps one of the most critical aspects of radiation hazards lies in these maximal permissible values. The existing evidence concerning the radiation dose/injury relationship makes it necessary for extremely low values to be recommended in almost all circumstances. For example, lead is one of the most toxic agents in orthodox industry, and the recommended maximal allowable concentration is 150 μg./m.^{3} of air. Uranium, on the other hand, is one of the least injurious radioactive elements, but the evidence when similarly treated makes necessary a maximal permissible concentration in air of 50 μg./m.^{3}. The maximal permissible concentrations of all radioactive substances in air, as recommended at present, lie between this value of 5×10^{-5} g./m.^{3} for uranium down to 3.7×10^{-11} g./m.^{3} for plutonium. The maximal permissible body burden of radium or plutonium is at present recommended as 0.1 μg., if there is to be reasonable safety. It is obvious that such extremely low values throw a very great burden upon design and ventilating engineers, management, supervisors, health and safety staffs, and operatives in industries where such risks may occur. Furthermore, the technical procedures needed to confirm that a radiation hazard is effectively controlled are frequently far more complex and laborious than those needed for other industrial hazards.

6. The Practice of Radiation Protection

Exposure to radiation or radioactive substances presents two types of potential hazard:

i. Exposure to injurious amounts of penetrating radiation from a source external to the body, as, for example, an *x*-ray installation, a gamma-emitting source, or a source of neutrons.

ii. Exposure to injurious amounts of radioactive substances contaminating the working environment and capable of being absorbed into the body, as radioactive gases, vapours, fumes or dusts through the lungs, as contamination through the gut from food, water or fingers, as solutions or foreign bodies through the skin, and, in extremely rare cases, as solutions through the eye surface.

If the occupational exposures resulting from both the above hazards are restricted to levels below the tissue injury threshold, as implied by adherence to the recommended maximal permissible exposures, then occupational radiation injury should normally be preventible. In practice, however, it is found that this requirement demands the solution of many difficult problems in order to ensure effective radiation protection, whether the operation is on a large, moderate or relatively small scale. These problems are similar in nature to those occurring in the elaboration of a protective policy against almost any toxic agent in industry or research. The main differences between radiation and other toxic hazards are due to the penetrant properties of the radiations, relatively low injury threshold of the body to ionizing radiation, and the fact that such radiations give no perceptible sensory warning of their presence, even at grossly injurious levels of exposure.

a. Preliminary Evaluation of the Radiation Hazards

Many large industrial, research, and medical establishments possess suitably qualified staff who are well able to evaluate the potential radiation hazards in a certain occupation or operation. Under other circumstances the small or inexperienced user may need to secure preliminary technical advice from the manufacturers or suppliers of the source of radiation, or from organizations with qualified staff available. In Great Britain, for example, the National Physical Laboratory, the Isotopes Division of the Atomic Energy Research Establishment, and the Medical Research Council, among others, are

well able to give such advice. As with other types of hazardous agent, it is now common practice for suitable guiding instructions to be issued and emphasized at the same time as the source of radiation is supplied.

b. Planning Methods of Operation

The planning of satisfactory methods of operation is without doubt the most critical phase of the radiation protection campaign. It may at times involve specially designing or altering the structure, facilities, equipment and operational procedures of the buildings concerned. Technical advice on such matters is usually available from suitable organizations. Properly applied, planning measures may well be able to control effectively the external radiation exposure of operatives, and ensure restriction of contamination of the working atmosphere or environment to safe or negligible levels.

In general, external radiation exposures are controlled by the siting of radiation-absorbent shielding between the source and the operatives, by increasing the distance between source and working position, by reducing the time required for the particular operation, by reducing the size and activity of the source as far as possible, or by a combination of these methods.

Freedom of the work areas and atmosphere inside the buildings from injurious contamination can be ensured only by sound design of working facilities, equipment, containers, general ventilation and air-extraction, well-planned operational methods, and by consistently good " housekeeping " in the building and in the conduct of laboratory experiments. The implication of Sir Thomas Legge's third postulate, that most industrial poisonings are likely to arise from the inhalation of toxic materials, is also likely to be true for radioactive substances. Special care is usually necessary to ensure complete control of atmospheric contamination, both for health reasons and for technical reasons connected with " background " activity measurement.

c. Training and Supervision of Operatives

The fact that ionizing radiations are not perceptible by any of the senses naturally tends to produce laxity in individual operatives' methods unless pre-operative training and subsequent education and supervision have convinced workers that they must conform to consistently clean, orderly and safe working methods.

For certain types of work, and where design and planning of operational methods and facilities have not been able to ensure control of the latent hazards, it is advisable to insist on the use of suitable personal protective equipment for operations which remain potentially hazardous. These may include, for example, rubber or lead-rubber gloves and aprons, footwear for preventing dissemination of contamination outside the area, laboratory coats or complete overalls and headgear to prevent personal contamination. Emphasis may also be required on the necessity of ensuring that all adherent radioactive contamination of the hands is removed by assiduous washing, especially of the fingers and nails. In some hazardous operations it is necessary that the operative be further protected from inhalational risks by wearing a suitable dust or canister respirator or, for greater comfort and greater safety, a supplied-air respirator.

There is, however, an upper limit to the extra safety gained by wearing personal protective equipment, in view of the restrictions imposed on movement, dexterity, vision, speech, thermal comfort or physical endurance. It is far better that these restrictions be avoided, wherever possible, by modifications at the stage of design and planning of the operations.

d. Hazard Detection and Measurement

In large specialized organizations, hazard detection and measurement is the main function of the so-called ' Health Physics ' team. In small organizations there is almost always sound reason for similar measures to be put into effect on a reduced scale.

One of the more important tasks under this heading is to confirm that the external radiation exposures of individual operatives fall within the maximal permissible values recommended for that type of radiation and circumstance. For this purpose the operative wears either the dental size photographic monitoring film, subsequently developed and assessed by comparison with calibrated standard films, or the " fountain pen " or " thimble " type of personal ionization chamber, which has a purpose similar to the film, but is usually adopted for the sharper, briefer radiation exposures. It is important to note that these individual monitoring measures do not record any but external radiation exposures ; it is possible to inhale or ingest an eventually lethal amount of radioactive substance from environmental contamination, and still be shown as ' within tolerance ' on the film.

The degree of atmospheric or other contamination of the working area is therefore frequently of the greatest importance. It is usually determined by the subjection of samples collected from a known volume or area of the environment to radioactivity " counting " with a view to comparing the recorded count with the maximal permissible values to be adopted for that particular aspect of the occupational environment.

7. Health Supervision

Where, in spite of all reasonable precautions having been taken on the above lines, a potential hazard still remains, due to the possible occurrence of undetected radiation exposures, or deviations from normal cycles of operation, or where biological confirmation of safe operational methods is required, health supervision is desirable. However, the preventive role of health supervision should not be over-stressed, as the greatest contribution to radiation protection obviously comes from physical, engineering and operational considerations.

Medical supervision may involve the placing in suitable jobs of workers having a confirmed or suspected pathological condition of the skin, blood, lungs, bone, excretory channels or other system susceptible to radiation injury. In general, the objective is to avoid possible injury from the additive effects of an existing disorder and ionizing radiation within the tissues. Particular emphasis is therefore necessary upon possibly pre-malignant conditions, chronic inflammatory reactions, or other states which may result in lowering the injury-threshold of the individual. The onset of specific radiation injuries should be detected as early as possible,but the diagnosis of very early leukaemia, leucopenia, bronchial

carcinoma or even bone changes due to radiation is hardly within the province of routine periodic examinations carried out by solely clinical methods. The value of such examinations appears to be limited to observations upon the general health of workers, the exclusion as far as possible of known early symptoms of occupational disease, inspection of the exposed skin, and examination for the continued suitability of the worker for his job. Periodic examinations also give valuable opportunities for emphasis upon the importance of the individual's contribution to his own protection from radiation hazards, for counteracting the occasional worries and misapprehensions which arise in the minds of operatives concerning the effects of such work upon health, and the occasional gathering together of all data upon health supervision for that particular person.

The clinical examination usually needs to be supported by special investigations. Haematological investigations are required in order to detect early response of the blood-forming tissues to radiation exposure, but the assessment of the results must be made with due care. The recorded blood count is influenced by a variable element of technical inconsistency and by a wide range of physiological variation between different individuals, or between the counts obtained at different times from the same individual. Progressive trends towards hypoplasia, the presence of immature cells in the circulating blood, or abnormally low counts may be of significance, even in the absence of known over-exposures. Radiography of the lung fields gives information of value in ensuring that only suitable operatives are placed on tasks involving a potential inhalation risk. Specific tests are in some instances available for the estimation of the individual's degree of absorption of radioactive substances into the body. These tests include, e.g., radiometric analysis of the urine, faeces, sputum or exhaled air, the determination of the gamma-radiation emitted from radium deposited in the bones of radium workers, or from the thyroid glands of persons exposed to radio-iodine. These are specialized tests, best carried out by suitably equipped and experienced organizations, with due care in the interpretation of the results obtained.

It is clearly important that in workers exposed to radiation, any complaints possibly arising from early radiation injury to the blood, skin, lung or bones should be thoroughly investigated; this becomes of increasing importance as the total duration of occupational exposure increases. Similarly it may be advisable that the known tendency of the heavy elements to be deposited excessively in calcium-deficient bones be counteracted by appropriate preventive dietetic therapy. Animal experiments indicate that immature bone may respond more seriously than adult bone to similar degrees of irradiation or exposure, and young persons exposed to radiation occupationally may need special care and health supervision.

Where relative over-exposure to radiation has been detected or suspected, or where the health of the operative for some reason is below an acceptable standard of fitness, it is advisable on preventive medical grounds to ensure an appropriate period of freedom from further radiation exposure, in order to prevent cumulative tissue injury. Decontamination and first-aid facilities may be needed for the rapid removal of contamination from the normal or injured skin, and for the treatment of possible aspiration of radioactive material into the mouth and thence into the stomach.

On the exclusively therapeutic aspect of radiation injuries there are few advances to be reported. The treatment of the radiation syndrome is described in the article [1] which follows. The treatment of chronic occupational radiation injuries such as early or established leucopenia, leukaemias, skin changes, bone manifestations and lung carcinoma remains based on existing medical or surgical principles for these conditions. Experimental work has been carried out on the prevention of biological sequelae from excessive bone contamination by radioactive heavy metals. The decalcifying and recalcifying therapy used in the past for lead and radium poisoning cases has been re-investigated, and also the use of the relatively non-toxic element zirconium in the early stages of heavy element absorption and deposition. Zirconium appears to behave as a competitor with the contaminant metal for preferential fixation within the bone. A further approach lies in the method of "isotope dilution". It is suggested, for example, that heavy dosage with stable iodine (^{127}I) immediately after or during over-exposure to radio-iodine (^{131}I) may proportionately dilute the contamination of the thyroid gland with the active isotope, and thus decrease the possible over-irradiation of the gland and adjacent tissues. Apart from these experimental measures, the therapy of imminent or established chronic radiation injury has not advanced materially in the past decade.

The extent and nature of the radiation protective precautions to be taken in the interests of occupational health naturally vary with the specific circumstances, but are particularly dependent upon the type and magnitude of the source of radiation concerned. In certain instances, work with small amounts of the less hazardous radio-isotopes may be safely carried out merely by suitable planning of the modus operandi and ensuring appropriate training of the operatives. In such cases, normal laboratory or work-place procedures, if of consistently good standard, may serve to control all the risks. In a greater proportion of cases, suitable design, planning, supervision, training, and hazard detection and measurement are needed to ensure occupational health. In the remaining instances, usually in large establishments concerned with nuclear physics research and development, or large-scale radioactive material utilization, the full and elaborate system described above has been found advisable in order to ensure continued occupational health among the operatives.

With reference to the medicolegal aspect of radiation hazards, and in addition to the general provisions of the Factories Acts, a Statutory Instrument already exists in Great Britain covering employment and occupational health in the luminous paint industry, the Factories (Luminising) Special Regulations, 1947. The Radioactive Substances Act, 1948, empowers the Ministries concerned to create further legislation to ensure the safeguarding of health amongst almost all groups of the community occupationally or otherwise exposed to radiation. The majority of potential radiation injuries are listed as "Prescribed Diseases" in the National Insurance (Industrial Injuries) Act, 1948.

Finally, it should be emphasized that in all the occupations and circumstances discussed in this paper there are many other possible ways of receiving an injury as severe as that from over-exposure to radiation. A due sense of perspective is necessary throughout the conduct of a radiation safety programme, in the interests of both the individual operative and of society.

[1] Loutit, p. 64

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TREATMENT OF THE RADIATION SYNDROME

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1 Physical action of radiations
2 Biological action of ionizing radiations
3 Prevention of damage due to radiation
4 The radiation syndrome
5 Treatment of the radiation syndrome
a Immediate shock and radiation sickness
b Intermediate latent period
c Period of delayed effects
d Period of recovery or subacute period
References

Diagnosis precedes treatment. This well-known medical precept presupposes that by diagnosis one means a full and thorough understanding of the pathology of the process in question and of all the physiological and biochemical disturbances involved. In the case of the radiation syndrome this criterion cannot be satisfied. The clinical course of events is well documented. The morbid anatomy and histology have been fully described. The fundamental actions of the ionizing radiations are largely known. In spite of all this knowledge, however, a thorough understanding of the disturbances caused is lacking.

1. Physical Action of Radiations

The subject of the physical action of radiations has been discussed at length by Lea (1946a). Radiations of certain wavelengths in their passage through matter can excite molecules. Such is the case with ultra-violet light. Other radiations, like *x* rays, artificially produced by the bombardment of selected targets with electrons, exert a much more disruptive effect on matter through which they pass. Not only is there a resulting excitation of the molecules, but electrons are actually ejected. This leaves a positively charged remnant, or ion. Hence radiations which have this effect are known as "ionizing radiations". The *x*-ray quanta exert their effect through the production of electrons along their path, and it is the electron which has this ionizing effect. The γ rays from naturally radioactive substances have an action similar to that of *x* rays; but being usually of greater energy than *x* rays they are more penetrating. β rays, being electrons, also exert an ionizing effect but are only feebly penetrating; α rays are positively charged helium nuclei and are still less penetrating but far more densely ionizing. Neutrons, being uncharged particles, are far less easily stopped; but when they do strike a target they displace charged particles, usually protons or hydrogen nuclei, which also are densely ionizing.

2. Biological Action of Ionizing Radiations

The action of ionizing radiations on living cells has been dealt with by Lea (1946a) and also in an earlier article in the Bulletin (Lea, 1946b). The vast bulk of the living cell is composed of water. The action of these radiations on water is therefore of the greatest interest. Weiss (1944) gives the following equations:

$$H^+OH^- + \text{radiation} \rightarrow H + OH$$
$$H + OH \rightarrow H_2O$$
$$H + O_2 \rightarrow HO_2$$
$$2HO_2 \rightarrow H_2O_2 + O_2$$

These are not the only reactions which take place. Nevertheless OH, HO_2 and H_2O_2 are all intensely oxidizing substances. One theory suggests that one result of the irradiation might be the oxidation of materials essential for cellular function, such as enzymes with sulphydryl groupings. This is the chemist's view-point.

For the cytologist, the most notable result of irradiation is damage to the nuclei of tissue cells. At mitosis, breaks in the chromosomes are observed. These breaks may undergo restitution, but they may also show cross union and other abnormalities. Such abnormalities are in many cases lethal to the cell, or may result in impaired physiological function. It was originally thought that these breaks were due to the physical passage of the ionizing particle cutting the chromosome like a hot knife. But this explanation may not be valid since chemical toxins, such as mustard gas and its derivatives, have also been shown to cause breakage of chromosomes (Darlington & Koller, 1947; Slizynska & Slizynski, 1947). Both radiation and chemicals may, however, produce this effect by a chemical disturbance of the anabolic-catabolic balance in the chromosome.

3. Prevention of Damage due to Radiation

If the mechanistic hypothesis that all the damage was due to the "hot knife" action of ionizing particles were correct, there would seem to be no adequate treatment; the only hope would be to prevent the particles from reaching sensitive cells. This is the present basis of protection against externally applied radiation. Adequate thicknesses of material of high density, like lead or concrete, can be made to absorb the radiations before they reach the body. *X*-ray tubes, cyclotrons and atomic piles are now surrounded by such protective screens to prevent damage to the operators.

The chemical hypothesis would appear to hold out greater hopes. It is true that so far no substance has been shown experimentally to have any therapeutic value. On the other hand claims are now being made with some confidence that certain chemical substances may have a protective value. Patt *et al.* (1949) have shown that the amino-acid cysteine, containing the —SH group, will diminish the mortality rate of rats exposed to supra-lethal doses of *x* radiation. This would be in line with a previous claim that glutathione had a protective effect against the radiation sickness produced by radiotherapy. It would also agree with Dale's findings (1947) that, in vitro, thiourea was highly protective to the enzyme carboxypeptidase. Flavanones have also been claimed as effective in preventing death of dogs from a median-lethal dose of *x* irradiation. Rekers & Field (1948) and Field & Rekers (1948) have demonstrated this effect with lemon-peel extract, rutin (a flavone-glucoside) and hesperidin (a methoxy-flavone glucoside) but not with ascorbic acid.

Rutin did not protect their experimental rats nor the mice of Cronkite, Eltzholtz, Sipe, Chapman & Chambers (1948). The former suggest that the substances with vitamin P activity delay the rate of vascular degeneration, but as to the exact mechanism they have no data.

The presence of oxygen in solution in water favours the production of HO_2 and H_2O_2. A diminished oxygen tension might therefore be expected to be beneficial. Shack & MacDuffie (1949) have shown that the erythroid elements of the bone-marrow of Swiss Bagg mice, conditioned to a low atmospheric oxygen tension, were more resistant to lethal doses of *x* rays than those of mice in normal atmospheric conditions.

This result may have another explanation. The low oxygen tension stimulated a hyperplasia of the marrow. Jacobson *et al.* (1948) had previously shown that a hyperplastic marrow may exert some measure of protection. Their rabbits, made anaemic by repeated bleedings or by haemolytic drugs, had an increased resistance, which at the time was unexpected. However, Treadwell, Gardner & Lawrence (1943) had earlier found that oestradiol benzoate had some protective action in Swiss mice against lethal doses of *x* rays. To be effective it had to be given about 10 days before exposure. They suggest that degeneration of the lymphatic tissue was induced by the oestrogen, and that by the time the radiation was given the lymphatic tissue was undergoing hyperplastic repair. Similarly, Cronkite, Sipe, Eltzholtz, Chapman & Chambers (1948) have shown that Swiss mice previously conditioned by 3 sub-lethal doses of radiation were, one month later, more resistant to lethal doses than control mice. Although they do not suggest it, it would seem likely that in these conditioned mice both the haemopoietic and lymphatic systems were in a reparative state of hyperplasia.

The suggestion that hyperplastic tissue may be more resistant than normal is somewhat paradoxical; for, by and large, the sensitive parts of the body are all relatively undifferentiated tissues undergoing frequent replacement. In any case, there is no suggestion so far as to how this observation can usefully be applied.

Whereas the oxidative effects of the products of the breakdown of water to produce hydroxylations (Stein & Weiss, 1948a) and deaminations (Stein & Weiss, 1948b) of organic compounds detectable by chemical methods require doses of *x* rays in excess of lethal doses by factors of thousands, this does not necessarily invalidate the chemical theory of the destructive action of the radiation. Mitchell (1943), for instance, has shown that therapeutic doses of *x* and γ rays cause a delay in the transfer of cytoplasmic ribonucleic acid to nuclear desoxyribonucleic acid.

In the present state of lack of knowledge, all prophylactic measures should be taken to provide competitors for the oxidizing agents. These easily oxidizable competitors, be they cysteine, glutathione or similar substances, must be non-toxic, water-soluble and capable of being absorbed into the water of the cell and even into the water of the nucleus if they are to compete successfully for the oxidizing radicles which are presumed to damage the essential nuclear material.

4. The Radiation Syndrome

The atomic bombs dropped at Hiroshima and Nagasaki resulted in tens of thousands of deaths. The vast majority of these deaths were due to multiple causes, of which, however, trauma, burns and the radiation syndrome were the most important. Previously the radiation syndrome was seen in man mainly following radiotherapy, in which only in exceptional circumstances is the radiation applied to the whole body. In Japan the widespread dislocation of all social services made careful observation and control of the casualties impossible. In radiotherapy it is the sick who are being exposed to radiation. In neither case, therefore, is there a clear-cut picture available. Some idea of the clinical findings in Japan are given by Warren (1946), LeRoy (1947), Tsuzuki (1947) and Howland & Warren (1948).

The picture of radiation sickness after radiotherapy is described by Whitmore (1943) and Shorvon (1949). The story can be supplemented by experiences with experimental animals. A considerable amount of work was carried out recently in the USA during the days of the Plutonium Project and reported by Painter *et al.* (1947), Prosser & Moore (1947) and Prosser *et al.* (1947).

A synthesis of these studies shows that there appear to be four clinical stages:

(*a*) *An immediate shock-like state* if the doses are sufficiently large. With supra-lethal doses experimental animals may even die "under the beam" (Henshaw, 1944). With mid-lethal doses, either immediately or with only a short latent period, comes the classical "radiation sickness" so well known in radiotherapy, with nausea, vomiting and prostration and lasting about a day or so.

(*b*) *An intermediate latent period.* The symptoms of the radiation sickness pass off. Experimental animals may appear superficially to be quite normal. This period varies with the dose given, and may be from a few days to a month—the greater the dose, the shorter the period.

(*c*) *The period of delayed effects.* This is a period of fever often leading to hyperpyrexia. There are dramatic and general signs of intoxication—weakness, prostration and loss of weight. Many cases show signs of aplastic anaemia—agranulocytic angina and indolent ulcerations, petechial and larger haemorrhages (melaena, epistaxis, menorrhagia and haematuria). Infections are common (Warren, 1946) and bacteriaemia is a frequent finding (Bennett *et al.* 1949). This stage appears to be of later onset in man than in animals: the longer it is delayed the better would appear to be the prognosis.

(*d*) *The period of subacute sequelae.* Those that survive the effects of this delayed damage present a subacute picture. Anaemia, weakness, persistent infection and emaciation predominate. Death or apparent recovery are possible.

5. Treatment of the Radiation Syndrome

Cronkite (1949) makes the point that the treatment of the single case can be "idealized"; in military practice the principle of the greatest benefit for the largest number operates. For theoretical reasons, however, it is more instructive to take the single case.

a. Immediate Shock and Radiation Sickness

The physical liberation of the energy is immediate on the explosion of the bomb. Histologically, damage to the tissues (the bone-marrow for instance) can be detected after the first half-hour. Mitosis has then ceased and severe degeneration of cells is notable at the third hour (Bloom, 1948). If, therefore, prophylactic treatment is not practicable, as was the

case at Hiroshima, there would appear to be no specific therapeutic action that can be taken. If prophylaxis is possible, as before radiotherapy, there are various substances that can logically be given or which have been found empirically to alleviate the side-effects of " radiation sickness ". Cysteine and glutathione have already been mentioned as competitors for the oxidizing agents formed from water, but presumably they would also act in the tissue to be irradiated and therapeutically might therefore be undesirable.

The onset of radiation sickness has been shown to be associated with a fall in levels of serum cholesterol by Holmes (1941), and with chloride depletion by Goldman (1943). Premedication with cholesterol and sodium chloride would therefore be sound. Tissue destruction may release histamine. This theory was supported by Ellinger (1945). Ellis (1942) has claimed therapeutic benefits from the use of histaminase, and Lofstrom & Nurnberger (1946) from an antihistamine agent, benadryl. Painter *et al.* (1947) showed by transfusion experiments that the blood of irradiated rabbits contained a depressor substance, but they could not confirm the efficacy of either histaminase or an antihistamine agent in treatment.

It is fairly well established in radiotherapy that radiation sickness is most pronounced when large areas of the body are irradiated, or when the neck or abdomen is involved. This may be due to some action on the autonomic nervous system and on the large ganglia or adrenal glands. Pressor substances, amphetamine (Jenkinson & Brown, 1944) and adrenaline (Painter *et al.* 1947) have been administered with the desired effect. If the effect were mainly on the adrenal cortex. exhaustion of adrenal cortical function might be expected. Ellinger (1947) and Ellinger, Roswit & Glasser (1949) claim that this is the case, and produce evidence that desoxycorticosterone is protective.

Deficiencies, especially of the water-soluble vitamins, have also been incriminated, and pyridoxine as a prophylactic is highly regarded by some radiotherapists (Shorvon, 1949). As pyridoxine has also been recommended in the treatment of agranulocytosis (Cantor & Scott, 1944) its worth cannot be ignored. Goldfeder *et al.* (1948) claim from its use increased survival of white mice exposed to lethal doses of radiation but found no significant differences in leucocyte counts. The latest claim is that a preparation, " Dramamine " (β-diaminoethyl benzhydryl ether 8-chlorotheophyllinate), is effective if given after sickness has started (Beeler, Tillisch & Popp, 1949). Its effect cannot be wholly explained by its antihistamine activity. The multiplicity of agents suggests that none is specific and that the causation of the syndrome is extremely complex. This is readily understandable.

One thing appears certain : this shock-like state is dissimilar from that of traumatic shock, about which current opinion inclines to a unitary theory of initiation from oligaemia (Gregerson, 1946). No diminution in plasma volume has been found in irradiated rabbits (Painter *et al.* 1947).

If, then, the shock-like state is due to some form of chemical toxin, as appears most likely, treatment must be aimed at general supportive measures. Complete rest in bed with full nursing routine is obviously desirable. Intake of food and water is usually voluntarily restricted. Rest for the gut may well be desirable as the intestinal mucosa, being one of the most radiosensitive tissues of the body, is grossly affected. From the work of Le Blond, Stevens & Bogoroch (1948) one can deduce that the turn-over of mucosal cells is about once every 24–48 hours, and Barron (1945) has shown that there is inhibition of the absorption of glucose from the gut after irradiation. Intravenous administration of glucose saline would therefore be useful at this stage, but because of increased capillary permeability caution is required.

b. Intermediate Latent Period

In this stage, while symptoms may be minimal, the signs in the peripheral blood are progressing (Prosser *et al.* 1947 ; Lawrence, Dowdy & Valentine, 1947). The lymphocyte count will have already fallen in the first stage. The polymorph leucocytes may initially have increased in numbers but now also fall calamitously. The greater the dose, the faster and more profound is the fall. It is suggested that in man minimal total leucocyte counts below 600 are always fatal, whereas counts above 1,500 usually indicate future recovery (LeRoy, 1947). This gross leucopenia is due to the destruction of red bone-marrow and of the lymphopoietic tissues. The logical treatment would be replacement therapy with preparations of concentrated leucocytes, for instance, the " leucocyte cream " from freshly drawn blood which has been centrifuged. Whole blood transfusions, except perhaps of leukaemic blood, would not supply sufficiently large numbers of leucocytes ; and leukaemic blood would not seem desirable on general principles. Moreover, it is thought that the life-span of the leucocyte in leukaemia is shorter than normal. The normal life-spans of lymphocytes and polymorphs have only been inferred from indirect experiments (Lawrence *et al.* 1947) ; they are, roughly, 5 hours for lymphocytes and 5 days for polymorphs. There is no evidence about the length of life of leucocytes present in leucocyte cream. On general grounds one would expect them to be damaged not only by the trauma but also by the chemical anticoagulant. Moreover, recent experimental work with rabbits by Weisberger, Heinle & Hannah (1949) suggests that infusions of fresh leucocytes suspended in Tyrode's solution produce an immediate leucopenia in the recipient. These leucocytes were, however, from an inflammatory peritoneal exudate. The logical treatment, therefore, may not be satisfactory in practice.

Apart from this form of replacement therapy, the recommended measures once again are general and supportive—rest and careful nursing ; an easily assimilated, low residue diet ; and an adjusted fluid balance. The chief requisite is the avoidance of any form of sepsis. Skin sepsis at pressure points and at needle punctures has particularly to be avoided, *secundum artem.* Spontaneous sepsis in the mouth, throat and intestinal tract has to be anticipated. Oral hygiene should therefore be given special consideration : penicillin lozenges and liquid paraffin are preparations which the present author would advocate. Intestinal bacteriostasis by suitable sulphonamides might also be indicated, provided that the necessary B vitamins are given by other routes. However, Cronkite and his collaborators (cf. Cronkite, 1949) obtained no benefit using this method in mice. Finally, prophylactic antibiotics are obviously indicated ; long-acting penicillin should certainly be given. Further experimentation with animals will show whether other antibiotics, alone or in combination, are preferable. Recent reports suggest that aureomycin has proved satisfactory. As this is given by mouth it has much to recommend it, in that needle punctures are avoided. Its use would also facilitate the handling of multiple cases.

c. Period of Delayed Effects

From the published reports of observations in Japan, it would seem that when the latent period was short (one week or less), the prognosis was extremely poor. Death seems to have been due mainly to alimentary disorders—diarrhoea, melaena, and subsequent exhaustion. When the latency was two weeks or more, intestinal symptoms, though present, were less severe and deaths seem to have been attributed largely either to haemorrhage or sepsis. The prevention of sepsis has already been discussed; the treatment of established sepsis would be similar but more intensive.

In addition to the leucopenia which by this stage (3rd to 4th week) has reached its nadir, thrombocytopenia and anaemia will have appeared. Clinical opinion of recent years has been very emphatic that even a slight lowering of the circulating haemoglobin is disadvantageous to the patient with sepsis. Transfusion of whole blood or of concentrated red cells will, therefore, have been indicated towards the end of the latent period or at the beginning of this period. Blood should be given in sufficient quantity and sufficiently often, daily if need be, to keep the haemoglobin level within normal limits. There is not only the accumulation of effete red cells but also a haemolytic process to be countered (Schwartz *et al.* 1947). For this purpose blood stored even for several weeks in a reputable preservative diluent, like acid citrate dextrose (Loutit, Mollison & Young, 1943), will be adequate. On the other hand blood has been recommended not only for its content of red cells but also for the natural protective globulins of the plasma. Any such beneficial effect of blood transfusion is much less well documented; but if the thesis is accepted, fresh blood would then be preferable to stored blood because of the diminution of labile factors during storage. It might be advisable to fortify the blood for transfusion with the known protective fractions of plasma such as γ-globulin (Mulford, 1947). In some animals at least, dogs for instance, abnormalities develop in the partition of the plasma proteins (Muntz, Barron & Prosser, 1946). If this is proved to occur also in man there would be indications for the additional infusion of whole plasma or selected plasma-fractions like albumin. There are suggestions that man may in fact be like the dog in this respect, in that oedema does seem to be a factor in the fully developed radiation syndrome. This being so it is imperative, when intravenous therapy is being much recommended, that the fluid balance and the state of the circulation be kept constantly under review.

In addition to the prophylaxis and treatment of sepsis, one has to combat the haemorrhagic tendency which is prominent in this period. In its slightest form, it may be manifested by a light petechial rash: at the worst, there may be calamitous haemorrhage. It has been pointed out that multiple factors are involved—the thrombocytopenia due to the aplastic anaemia, the damage to capillary walls and the possible presence of circulating anticoagulant. The thrombocytopenia is also best treated by replacement therapy, i.e., by transfusion of fresh blood or fresh plasma-leucocyte-cream. Unfortunately, the beneficial effect, as in essential thrombocytopenia, is likely to be transient, so that frequent, perhaps daily, transfusions may be needed for such cases too. The capillary fragility can be handled prophylactically and therapeutically by the administration of vitamin P and analogues. The circulating anticoagulant, thought to be heparin or something like it, can be counteracted by protamine or toluidine blue (Allen *et al.* 1948). It is disappointing to record that in Allen's experiments, though the haemorrhage was controlled, the dogs nevertheless died. Moreover, while protamine is usually regarded as bland, toluidine blue is toxic to dogs, though apparently not acutely so to man. It is, however, not dissimilar to trypan blue, which has delayed toxic effects in animals.

Whatever the specific treatment, the general treatment of the haemorrhagic tendency will once again include blood transfusion as replacement therapy. It is notable that blood transfusion is indicated on many grounds; it is the one therapeutic measure that seems to have won universal approval. Yet there is no experimental demonstration that treatment by blood transfusion improves the chances of survival in the radiation syndrome. The results obtained by Cronkite (1948) from his observation of goats exposed to radiation from the atomic bomb at Bikini were equivocal and the experiment was admittedly uncontrolled.

The whole picture of the effects in this delayed period suggests that in animals, and probably also in man, sepsis or haemorrhage is usually present, but that death is not directly attributable to these causes only. There seems to be in addition a general metabolic failure. One aspect of this may be the extreme negative nitrogen balance in the terminal period, reported by Prosser *et al.* (1947). There is, however, no valid explanation why this failure of nitrogen metabolism is not immediate, but delayed. It is thus not the same as the catabolic crisis seen after mechanical trauma. It has been, therefore, usually attributed to "toxaemia", either bacterial or anaphylactoid. The anaphylactoid hypothesis has certain features which commend it—the time of onset (when the dose is near the median lethal) and the probability of liberation of histamine and heparin; but, in doses above the median lethal, death occurs earlier and so before the manifestation of the anaphylactoid phenomena; the latter, then, at best can be only a part of the picture and are not the fundamental cause of the metabolic failure. The Chicago workers (Bloom, 1948; Hagen & Simmons, 1947) have observed in experimental animals a periodicity both in the pattern of deaths and in the cytological responses (e.g. in the marrow). It would appear that regeneration of damaged tissue may proceed through *formes frustes* before satisfactory replacement is maintained. This suggests a possible deficiency but no particular one has been identified.

d. Period of Recovery or Subacute Period

If those exposed to heavy doses of radiation survive, they recover but slowly. This seems to have been the experience in Japan, as it is after extensive radiotherapy. Lassitude and a failure to gain weight at the expected rate seem to be prominent symptoms. There may be some delay in the return of function of the haemopoietic tissue, with resulting anaemia. Persistent infection may also delay recovery.

The treatment during this period must be the same as that of any debilitating condition. Persistent infection needs its specific treatment. If this can be ruled out, every form of psychological encouragement should be given. In addition, a high calorie and high protein diet is indicated. In the case of the bone-marrow, although anaemia and leucopenia may persist, the marrow is usually at this stage hyperplastic. The condition therefore resembles some idiopathic and toxic refractory anaemias. It is easy to postulate vitamin

deficiencies but none can be identified. Nevertheless the usual supplements of known vitamins and the maintenance of a reasonably normal haemoglobin by blood transfusion are indicated on general grounds.

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* The letters MDDC and AECU, appearing above in references marked with an asterisk, stand for Manhattan District Declassified Code and Atomic Energy Commission Unclassified Documents, respectively. Information about these documents may be obtained from the United States Atomic Energy Commission, Document Sales Agency, P.O. Box 62, Oak Ridge, Tennessee.

INDUSTRIAL INJURIES

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1 Classes of injury
  a Cases treated in the factory surgery
  b Injuries causing loss of working time
  c Fatal accidents
2 Summary of statistics
3 Prevention of specific injuries
4 Advances in treatment
References

A study made in 1944 of accidents at three engineering works showed that about 7 % of workers were injured each day (Williams & Capel, 1945). This figure included all injuries, however slight, but it shows the vast number of traumatic incidents as a result of which expert and perhaps repeated treatment may be required ; some of the injuries cause loss of working time, some disability, and some death. We will first consider the clinical types and relative importance of these industrial injuries and then review briefly some advances in treatment designed to reduce the consequent human and material losses.

1. Classes of Injury

By far the largest part of British industry is concerned with engineering in metals. The studies discussed here deal chiefly with this field though the conclusions drawn could be applied to other industries, with suitable modifications. The injuries will be considered in logical sequence under three headings.

a. Cases Treated in the Factory Surgery

Of the very large number of injuries occurring in the workshop only a small proportion is seen in the factory surgery, possibly about one-seventh of the total if the figure of 7 % of workers injured daily be accepted. The proportion varies with the type of injury, the adequacy of medical facilities, and the attitude of the injured men to these facilities. In one engineering works employing 15,000 men it was shown that in 1949 an average of 172 fresh injuries, corresponding to rather more than 1 % of the workers, were reported daily. Another factory with 4,000 employees averaged, in the first six months of 1949, 45 new injuries per day, again a proportion of about 1 %. Trevethick (1949) reported a similar proportion among 6,300 steel workers.

The injuries in the engineering works mentioned above were analyzed and the results are shown in fig. 1. Of 1,031 injuries 61 % were cuts, lacerations, or puncture wounds. This was much the commonest type of injury. A similar finding was reported by Archibald & Whitfield (1947) who showed that 55 % of 444 surgery cases in an ordnance factory were cuts and puncture wounds. Further analysis of the figures obtained in the engineering works showed that one-fifth of these injuries were caused by splinters of wood or metal. A more striking feature is that 92 % of them were injuries of the hands. The other numerically important group was that of eye injuries which made up 20 % of the cases treated in the factory surgery. All but 1 % resulted from foreign bodies in the eye, and after removal of the foreign body further re-attendance at the surgery was not usually necessary, though a few cases needed repeated treatment. Kefalas (1948) reported a study of 14,722 such injuries occurring in shipyards.

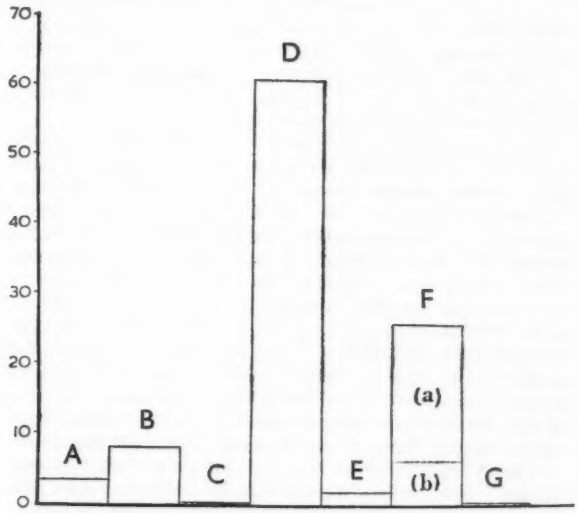
It was also shown that each injury reported required, on the average, just over one re-dressing ; that is, about two-thirds of the men attended only once and the remainder, on an average, three times. The number of re-dressings will vary between factories, differences in severity and type of injury and because of differences in surgical and nursing practice.

b. Injuries Causing Loss of Working Time

The statistics published by the Factory Inspectorate show that annually about 3 % of factory workers have injuries causing them to be off work for more than three days. The annual reports[1] of the Chief Inspector of Factories give excellent summaries of the general circumstances of these accidents and the industries in which they occur. The cost

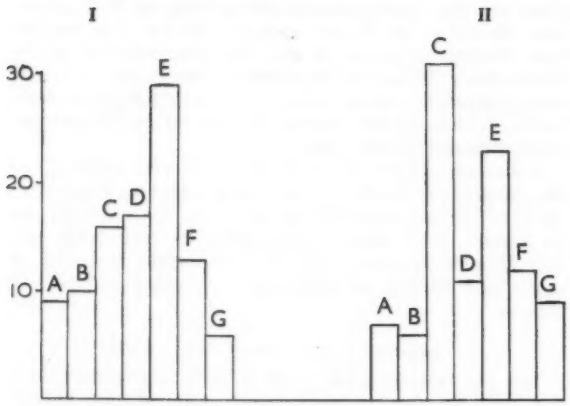
[1] Published by His Majesty's Stationery Office, London.—ED.

FIG. 1. PROPORTIONS OF DIFFERENT TYPES OF INDUSTRIAL INJURY AMONG 1,031 CASES TREATED IN A FACTORY SURGERY DURING 1949



Ordinates : Incidence as percentage of total
A : sprains
B : contusions
C : fractures
D : cuts, lacerations and puncture wounds
E : sepsis
F (a) : eye injuries
  (b) : other traumata
G : dermatitis

FIG. 2. PROPORTIONS OF INCIDENCE AND OF LOST TIME DUE TO DIFFERENT TYPES OF INJURY IN 307 COMPENSATION ACCIDENTS DURING 1946



Ordinates : Percentage of total

I = incidence
II = lost time

A : sprains
B : contusions
C : fractures
D : cuts
E : sepsis
F : other traumata
G : dermatitis

to the community of these accidents is very high ; the annual loss of working time has been estimated at 25,000 man-years (Ministry of Labour and National Service, 1949) and, even before the recent war, payments under the Workmen's Compensation Acts totalled between £6 and £7 million annually (Home Office, 1940) and the total cost, including disturbance of work and damage to materials, probably amounted to about £30 million per annum (Vernon, 1936).

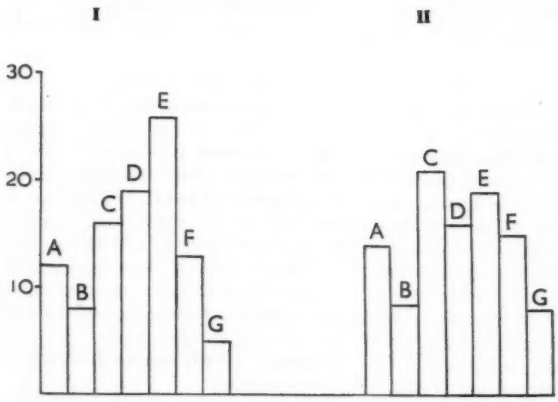
National statistics, as at present available, show only the number of accidents and are not corrected for hours of work or for numbers of men employed, nor do they give information on the amount of time lost. In accordance with the recommendations of the International Labour Office and the Royal Society for the Prevention of Accidents, many individual firms correct this deficiency by calculating an accident frequency rate per 100,000 working hours and a severity rate as numbers of hours lost (weighted for disablement, etc.) per 100,000 working hours. These indices are helpful for administrative purposes but are of little value when medical problems are involved. If we are to try to reduce the loss of time by improvement of treatment we must know what clinical types of injuries occur and which are most important.

A study on these lines in a light engineering factory employing 7,500 workers showed that in 1946 there were 307 "compensation accidents" (i.e., accidents causing a loss of more than three days). Of these, 29 % were septic injuries, 17 % cuts and lacerations, 16 % fractures, 10 % contusions, 9 % sprains, and 6 % dermatitis. Other injuries totalled 13 % and included burns (4 %) and eye injuries (2 %). This distribution is shown in fig. 2. The loss of time due to these 307 accidents was 9,590 calendar days and the percentage of this time attributable to each type of injury is also shown. The mean loss per injury was 31 days. Fractures, with their high mean loss of 61 days, accounted for the greatest amount (31 %) of lost time, but they were closely followed by septic injuries whose high incidence and mean of 25 days lost caused 23 % of the total loss. Of the other types of injury cuts caused 11 %, dermatitis 9 %, sprains 7 %, contusions 6 % and other injuries 12 % of the total loss of time. An outstanding finding, not shown in the figure, was the great importance of injuries of the hand. They accounted for 57 % of the total number and for 56 % of the time lost.

The study was repeated at the same factory for 1948 and showed similar proportional incidence (fig. 3), though the total incidence was down by 30 %, i.e. from 307 to 215, the numbers employed having remained materially constant. It therefore seems that the reduction was due to general rather than specific causes. The mean time-loss per injury was also reduced to 24 days so that the total time-loss, 5,098 days, was only a little more than half of the 1946 figure. The time-loss per injury was reduced particularly for sepsis (from 25 to 17 days), fractures (from 61 to 30 days) and dermatitis (from 42 to 35 days) and it was precisely for these conditions that advances in treatment had been introduced.[2] Possibly the proportion of septic injuries in this factory was higher than in the engineering industry as a whole, for which the Factory Inspectorate reports 10 % of compensation accidents as due to sepsis. On the other hand, many septic injuries in factories are not reported as such, and scrutiny of medical records shows that many injuries correctly recorded as e.g., lacerations, subsequently cause loss of time because they become septic. Since sepsis can usually be avoided, its prevention is very important.[3] The proportion of contusions

[2] See also Squire, Cruickshank & Topley, p. 28.
[3] See also Williams, p. 75.

FIG. 3. PROPORTIONS OF INCIDENCE AND OF LOST TIME DUE TO DIFFERENT TYPES OF INJURY IN 215 COMPENSATION ACCIDENTS DURING 1948



Ordinates : Percentage of total

I = incidence
II = lost time

A : sprains
B : contusions
C : fractures
D : cuts
E : sepsis
F : other traumata
G : dermatitis

and sprains has been found to differ in other factories ; together they may account for one-third of the compensation accidents in heavier industry. Burns also may comprise as much as one-fifth of the injuries in certain types of foundry, and eye injuries too are probably more important than the study suggests, since they accounted for 7 % of compensation cases in a large factory in 1949 where 15,000 workers were employed; this is in conformity with the national figure of 6 % in engineering in metals (Ministry of Labour and National Service, 1949).

Some of the accidents causing loss of working time also cause permanent disability. This problem is still being studied and it is not yet known which are the main types of injury involved. An idea of the frequency of such disablement can be obtained from the statistics published by the Royal Society for the Prevention of Accidents (1949). In 1948, 318 firms in electrical, automobile, and general engineering reported altogether 176 accidents causing permanent disability. These factories worked a total of 981,000,000 man-hours and had an over-all accident frequency rate of 1.8 (i.e., per 100,000 man-hours). Reports show that the total number of accidents was about 18,021 and hence the proportion of them causing permanent disablement was very close to 1 %. Assuming a 45-hour week, it follows that about 4 % of workers suffered an accident causing loss of working time and since for this purpose losses of less than three days are included the finding is consistent with the national figure of 3% for compensation accidents. The Factory Inspectorate recorded 110,952 compensation accidents in 1948 for the engineering group of industries, so it would appear that, annually, more than 1,000 accidents in this group result in permanent disability.

c. Fatal Accidents

The national statistics for 1948 showed 861 fatal industrial accidents. Of these, 552 occurred in factories—this figure being nearly back to its pre-war level after a rise above one thousand in 1941—and corresponded to one fatal accident per 12,000 workers per annum. The remaining 309 deaths occurred in docks, warehouses, and building and constructional operations ; the Chief Inspector of Factories points out that the number of fatal accidents for those industries has risen recently and is now higher than the pre-war level, for the same industries.

In order to ascertain the types of injury which caused these deaths the Coroner's records for industrial accidents in the Birmingham area were examined. The summarized causes of death of 321 workers who were killed in premises covered by the Factories Act, 1937 during the ten years 1940–49 were analyzed. Since many suffered several severe injuries analysis was not easy, but Table I shows a classification under what appeared to be the major injury.

An outstanding feature of Table I is the predominance of severe fractures, many of them involving the skull. An alternative grouping shows that head injuries totalled 118 (37 %), chest injuries 27 (8 %), and abdominal and pelvic injuries 23 (7 %). A striking finding is that 26 of the cases (8 %) died of complications of minor injuries and most of these were related to infection of wounds ; the 13 deaths from sepsis and the 6 cases of tetanus all followed small open wounds. Two small burns and two minor fractures also caused death after becoming septic ; of the remaining three cases, two were minor injuries of the legs in elderly people who developed gangrene and the third died of thrombophlebitis and embolism following a laceration of the leg.

TABLE I. ANALYSIS OF THE MAIN INJURIES IN 321 FATAL INDUSTRIAL ACCIDENTS (BIRMINGHAM, 1940–49)

Injury or illness	Number of cases	Percentage of total
Fractures :		
Skull	95	
Limbs	13	
Spine	12	
Ribs	12	145
Pelvis	11	
Other	2	
Other head injury	23	7.2
Contusion or crush :		
Chest	11	
Abdomen	2	19
Other	6	
Other intrathoracic injury ...	4	1.2
Other intra-abdominal injury ...	10	3.1
Infection of minor wounds :		
Sepsis	13	19
Tetanus	6	
Burns	26	8.1
Electrocution	10	3.1
Multiple injuries	37	11.5
Poisoning :		
Carbon monoxide	7	
Trichlorethylene	2	12
Other	3	
Silicosis	6	1.9
Asphyxia	5	1.6
Other injuries and diseases ...	5	1.6
Total ...	321	100.0

2. Summary of Statistics

The information on incidence and loss of working time which we have reviewed is as yet incomplete and is certainly subject to considerable sampling errors but, to summarize the kind of experience it indicates, let us consider an average engineering factory employing, say, 1,000 workers. Such a factory might have about 70 injuries occurring daily in the shops and, of these, 10 will be presented at the surgery for treatment. Most of them will be hand injuries, mainly cuts, and will need dressing. They may on an average require one re-dressing, so that dressing time per day will total perhaps two hours (Schilling, Roberts & Goodman, 1950). About every ten days one injury will cause loss of time of 10 to 20 days. Once in three years an injury resulting in some permanent disability may occur and about once in 12 years a fatal accident. Such a factory working a 45-hour week would record a frequency rate of 1.6 and perhaps a severity

rate of 500, values which occur commonly in the published statistics.

3. Prevention of Specific Injuries

Apart from measures to prevent the occurrence of accidents, such as are discussed by Whitfield in the succeeding paper[4], knowledge of the types of injuries which occur sometimes gives a lead to their specific prevention, even though the conditions causing the accidents may be beyond control. Examples are the use of asbestos spats and leggings by foundry workers to prevent burns of the feet by molten metal, boots with toe-caps reinforced by steel or stiff leather to prevent crush injuries, and the many types of goggles for the prevention of eye injuries (Ministry of Labour and National Service, 1940). In the past, the chief difficulty has been not so much in providing efficient protection but in providing it in a form which is acceptable to the worker. The greater attention now being given to this difficulty should result in fewer injuries. In general, however, preventive measures which do not demand individual co-operation are to be preferred.

4. Advances in Treatment

During the past ten years the treatment of both minor and major injuries has made notable advances. In many fields it has been possible to apply to civilian practice lessons learnt in war and these lessons have been supplemented by studies of the injuries found most commonly in industry. It is not appropriate to consider these advances in detail here, but mention will be made of some of the new techniques and of the facilities required for their application.

War-time experience in the closure of major open wounds has been confirmed in the treatment of civilian accident cases. Reviewing this subject, Essex-Lopresti (1950) summarizes the principles of modern practice : prompt surgical treatment, cleansing of the skin around the wound, excision of non-viable tissue, immediate closure by suture or skin-graft of early cases and abolition of dead space by pressure dressings. These principles are giving good results with compound fractures ; they are also applicable, with modification, to burns and less severe injuries. For example, early excision and skin-grafting of burns of full skin thickness, due to molten metal, is reducing the lost time and disability due to these injuries ; similar methods used for burns of the hand are described by Ross (1950).

The same principles have been applied to the common traumatic amputation of the finger through the terminal phalanx. Horn (unpublished observations) reports successful results with more than 100 such cases treated by an improved technique, based on the immediate skin flap grafting recommended by other authors (cf. Iselin, 1940), so that without lengthening treatment time, permanent disability has been greatly reduced.

The importance of small wounds and, in particular, sepsis of small wounds has been emphasized above. Williams' studies of the types and sources of such infection have been followed by the introduction of the no-touch dressing technique in surgeries and hospitals (Clayton-Cooper & Williams, 1945, and elsewhere in this number[5]). A further development has been a transparent vapour-permeable occlusive dressing which should prevent added infection between dressings and reduce the time spent at the factory surgery (Bull, Squire & Topley, 1948 ; Schilling *et al.* 1950).

Should sepsis become established, recovery can be helped by chemotherapy. For example, in a controlled series of 169 finger pulp infections, Harrison, Topley & Lennard-Jones (1949) demonstrated the value of a modified surgical technique combined with systemic penicillin in reducing the healing time and complications of these numerous and potentially dangerous injuries.

Suitable facilities are required for the effective application of the new techniques for reducing suffering, disability and lost time. It is well known that a factory surgery must be conveniently situated in the works, so that men will attend for treatment. The lay-out of the interior of the surgery which will best expedite dressings and minimize wound infection has been studied by Gissane, Miles & Williams (1944). For a group of smaller firms a mobile dressing station such as that described by Eagger (1948) may provide the best solution.

For the more severe injuries, hospital services are needed. An experiment is now being made with a mobile resuscitation and operating theatre so that treatment can be given on the spot to the very severely injured. For the more usual cases there is need for a general accident department providing early and efficient surgery, and so integrated with rehabilitation and industry that the surgeon can plan and achieve the quickest return of optimal function and that the patient should never lose sight of this goal (Gissane, 1944). Rehabilitation under continued surgical guidance, but within industry, is a promising method of approach to this problem. Two centres organized on these lines, associated with British motor-car factories, are giving good results (Plewes *et al.* 1948).

When these improved methods become generally available it should mean that the multiple minor injuries of industry will be more efficiently treated and, by the prevention of sepsis, fewer of them will cause loss of working time and fewer still cause death. The more severely injured should be back at work sooner, with less disability, and more of the very severely injured should survive.

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[4] Whitfield, p. 73.

[5] Williams, p. 75.

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NOTES ON THE CAUSES OF ACCIDENTS

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1 The need for records
2 Methods of analysis
3 General conditions
  a Working environment
  b Design of equipment
4 Individual conditions
  a Accident proneness
  b Emotional and social conditions
References

It can be assumed that, except in extraordinary circumstances, people do not wish to suffer injury. An accident is therefore a failure on the part of an individual to deal adequately with a specific situation. The extent of the failure need not concern us; particular situations obviously vary in the extent to which they offer opportunity for adequate behaviour (in the sense of avoidance of injury). There are situations about which great surprise is expressed when an accident occurs, and conversely there are situations in which an accident is regarded as inevitable.

1. The Need for Records

Any study of the causes of these failures, if it is to be of the slightest practical use, must go beyond mere expressed opinion. One of the most important questions which arises is: what features of the situation make an accident nearly "inevitable"? To answer this, the keeping of accident records which describe the accident situation and the resulting injury in systematic form becomes a necessity. Though the form of record found to be most useful will naturally vary in detail from industry to industry, in general the record should provide the following information:

i. *Details of the injured person*—name (and identification, such as works number), sex, age, occupation.

ii. *Details of time and place of accident*—hour, shift, day, week, year. Location (in some convenient classification, such as shop or department).

iii. *What the injured person was doing at time of accident*—a standardized classification of the various operations performed in the occupation.

iv. *What object, if any, caused the injury*—a standardized classification of objects appropriate to the occupation.

v. *Any other circumstances*, such as slipping, stumbling or falling; or the action of a second person.

vi. *Nature of injury*—according to the medical classification or the first-aid report.

vii. *Location of injury*—a mixed surface and skeletal classification.

viii. *Absence*—number of working days lost as a result of the accident up to, say, 30 days or more.

An example of such a system of records compiled for a specific industry is the "Non-Fatal Accident Return Under Coal Mines Act, 1911" (Ministry of Fuel and Power M.D., Return 39).

2. Methods of Analysis

Accident records provide the data for the study of accident causation. From the definition of an accident as a failure it is possible to go further. It may be primarily a failure on the part of the individual to perceive the risk, or primarily a failure to make the correct movement (particularly in work with tools); or it may be some combination of the two.

For example, a man who walks into a revolving shaft may have done so for one of several reasons: (i) he may not have seen it, his attention being drawn elsewhere; (ii) although seeing it, he may not have perceived that it was in motion, because of poor lighting conditions; (iii) having realized the danger he may yet have been unable to stop quickly enough to prevent running into it; (iv) having seen it and being in a position to stop, he may not have recognized it as a hazard. In the case of a revolving shaft, the last possibility is unlikely to apply to normal adults; but the recognition of risk is an aspect of industrial training which should not be neglected.

The analysis, therefore, can follow two major lines of investigation: (i) the study of the general conditions which affect the chance of failure, that is, affecting almost all workers and (ii) the study of differences between individuals.

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3. General Conditions

The first part of the analysis can be further subdivided into two parts: the working environment, and the design of equipment.

a. Working Environment

As an example of the approach to this aspect may be cited work on the relation between illumination and accident risk. Illumination directly affects the perceptual element in the accident situation, and may also relate to fatigue. Other environmental studies have also been made on the effects of temperature, humidity, hours of work, etc., and for most occupations it is now possible to lay down the tolerated limits for the environment. These effects are thoroughly discussed by Vernon (1936). More recent laboratory work relating temperature and humidity to failures in perceptual and motor performance is given by Mackworth (1950).

The effects of prolonged activity in a complex skill are given by Davis (1948), who, although dealing with aircraft accidents and not with personal injury, discusses the deterioration in the ability to perceive or to act upon displayed information, or to make appropriate controlled movements. He is also concerned with the individual differences in the nature of the deterioration.

b. Design of Equipment

Study of the more specific features of the accident situation is less well advanced, although a considerable number of *ad hoc* investigations have been made. These have mainly arisen from opinion, aided by observations of the frequency of accidents, that a particular lay-out or a particular piece of equipment is unnecessarily hazardous. Investigation of such cases can be considerably assisted by the study of accident records of the form suggested in Section 1 above. The discrepancy between the risk in the suspected situation and in other places in which the same work is done can often be traced to specific operations, and may receive corroboration from a study of specifically localized injuries. This information therefore defines the immediate problem, and focuses the attention of the equipment designer, safety engineer, training officer and others, on the origin of the hazard.

Comparative studies of accident experience between different types of equipment, or between different types of shop lay-out, should be a matter of routine, as large differences may exist without otherwise attracting attention. As an example (Whitfield, 1946) may be quoted the comparison of haulage accidents in three collieries, each working two seams, giving a total of six different working conditions. One of the six conditions had a record of only nine disabling accidents, whereas had the risk been equivalent in all conditions it would have shown the much higher number of 24.63 accidents. Analysis of injury by location showed that the comparatively small number was due mainly to a marked reduction in injury to hand or arm, and further that this was related to the operations of coupling and uncoupling tubs, and clipping or unclipping them from the rope. Inspection of the hand and arm movements in these operations revealed that the lay-out of the good condition had certain features not present in the other conditions, and these were responsible for its relative safety.

If similar comparative observations are kept in a systematic form it may at some later stage become possible to link them with laboratory "human engineering" observations, with the purpose of laying down general principles of machine design and lay-out best fitted to normal human capacities.

4. Individual Conditions

The other main line of enquiry has been into the question: why do some people have more accidents than others engaged on the same work? A general conclusion on the effect of age may be stated. The young worker has a high accident rate, which can be shown to be due to inexperience. It seems possible that improvements in systems of training in recent years will do much to reduce this high rate. In some occupations the markedly older men show an increase in accident rate. It is not easy to suggest specific reasons for this.

a. Accident Proneness

Even within homogeneous groups, e.g. of age, employment, environment, etc., there remain differences between people in their proneness to accidents. The original study of Greenwood & Woods (1919) and those of many later contributors, have shown this. The problem has been to discover what other human characteristics are involved. A break-down into the perceptual and the motor aspects is again relevant. The early work in this field mainly dealt with the relation of simple movement ability, or simple combinations of perception and movement ("reaction time"), to accident proneness. The correlation is low. Farmer & Chambers (1929) and Farmer, Chambers & Kirk (1933) obtained statistically higher correlations between accident proneness and the aestheto-kinetic tests, which demand a close co-ordination of the display and the controlled movement. Davis (1949) has suggested that "the cause of accident proneness lies in the failure of the response mechanism to be engaged by the stimulus". From the same investigation Whitfield (unpublished) has shown there are age differences amongst coalminers prone to accidents. The older accident-prone (40 years of age or more) are less capable than their contemporaries in controlled movement performance, whereas the younger accident-prone show deficiencies in perceptual tasks which involve observation and immediate memory of relationships. The correlations obtained in all studies do not suggest, however, any practical value in pre-employment selection to eliminate those prone to accidents, except in the most highly specialized tasks.

Some apparently accident-prone individuals repeat the same type of accident more often than would be expected by chance. This suggests that they have developed a hazardous combination of movements for a particular process in their work. It may be possible to re-train such individuals in the particular process involved and thereby reduce their personal susceptibility to accident.

b. Emotional and Social Conditions

Comparatively little is known directly about the relation of emotional or social conditions to accident risk. An enquiry into the hazards of war-time operational flying suggested that emotional factors were of more importance than fatigue (Reid, 1948). It is reasonable to argue that preoccupation will increase the likelihood of an individual failing to perceive an indication of hazard to which he would normally respond, and similarly to expect that emotional stress would militate against the production of adequately controlled movement. With respect to social conditions the difficulty lies largely in the ability reasonably to describe the social and

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PREVENTION OF SEPSIS IN INDUSTRIAL WOUNDS

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1 Bacteriology of wound sepsis
2 Source of the infecting organisms
  a Self-infection
  b Cross-infection
  c Modes of cross-infection
3 Prevention of wound infection
4 Organization of the factory surgery
5 Sepsis developing in untreated wounds
References

Sepsis is a common complication of industrial wounds; it is a complication that commonly results in a loss of working time, and not infrequently leads to some residual disability. Nor are the severe complications confined to the major injuries; many of the most serious examples of sepsis arise in wounds so trival that they are neglected at the time of infection.

The management of the major laceration, and its protection from pyogenic infection, lies in the province of the surgeon and the hospital, and will not be discussed at any length in this article. I propose, rather, to discuss research on the causes and prevention of sepsis in small wounds such as are commonly treated in the factory surgery, or in the hospital out-patient department. The emphasis will be laid on the bacteriological aspects of the problem, since these have formed the subject of most of the recently published work. The problems of treatment of established sepsis are considered by Bull elsewhere in this number.[1]

1. Bacteriology of Wound Sepsis

Clinical sepsis, accompanied by inflammation, swelling, and purulent discharge, is nearly always associated with infection by one or both of the pyogenic cocci, *Staphylococcus aureus* and *Streptococcus pyogenes*, these names being used to denote respectively coagulase-positive staphylococci and β-haemolytic streptococci of Lancefield's Group A. Thus Williams & Miles (1945), examining 487 wounds within two days after the first recognition of sepsis, or of incision of a closed abscess, isolated one or other of these microbes from all but 8% of the wounds, and there was some evidence that several of the few failures were due to technical difficulties. *Staph. aureus* was isolated from 86% of the wounds and was present in pure culture in 68%; the corresponding percentages for *Str. pyogenes* were 25 and 5 respectively. (See also Le Quesne, 1946.) *Staph. aureus* was found in all types of wound; in contrast, the proportion infected with *Str. pyogenes* differed with the kind of wound. Thus streptococci were rarely found in those lesions that were first seen at hospital as closed abscesses (pulp-space and web-space abscesses, suppurative tenosynovitis, etc.), or in wounds that had been septic for a few days only, but they were common in wounds that had been septic for some time, particularly in open and discharging wounds (such as paronychia).

Examination of septic wounds in factory surgeries revealed no notable differences from this picture. In all groups of wounds, sepsis due to coliform organisms was very rare, despite the frequent contamination of many machine lubricants with such microbes.

Williams & Miles (1949) made detailed bacteriological and clinical observations, both in factory surgeries and in a hospital out-patient department, on a considerable number of small wounds throughout their course, from the time of first treatment within a few minutes or hours of injury to the time of healing. It was clear from this study that the primary bacterial invasion of the wound was nearly always by *Staph.*

[1] See p. 69.

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psychological variables. Boredom may resemble fatigue in the behaviour it induces, but measures of boredom are not practicable. On the other hand " high morale " may reduce accident rates, even though we cannot define " morale ". Changing accident rates at different periods must be considered in relation to concomitant social or economic change. An increase in the accident rate does not necessarily imply a change in objective risk, nor need it imply " industrial fatigue ". Something of this nature would be true if all severities of accident were increased in frequency. If short-term absence is increased disproportionately it is more likely to indicate a lack of incentive to work.

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aureus; streptococcal infection usually appeared to be the result of a later, superimposed, invasion. Furthermore, staphylococcal infection of wounds was far commoner than was obvious from the prevalence of manifest sepsis; of small wounds treated in hospital, 19.6% developed sepsis or inflammation due to staphylococcal infection, but an additional 25% had "silent" staphylococcal infection, i.e. infection unaccompanied by clinical signs of disease.

2. Source of the Infecting Organisms

One major problem, then, was to determine the source of the staphylococci that were evidently initially responsible for the sepsis, and the time at which they entered the wound. We may distinguish, firstly, "self-infection"—in which the bacteria enter the wound from some normal carrier site (nose, throat, or skin) or some infected wound on the patient himself—from "cross-infection", in which the bacteria are derived from sources elsewhere in the environment. Such environmental sources include carrier sites on chance contacts and on the medical personnel who treat the wounds; the infected wounds of other patients being treated in the same department (and, indeed, of the medical staff); and such fomites as contaminated bedclothes, surgical equipment, and floor dust.

It has already been noted that infection, both silent and manifest, is so common in wounds that any wound, whether it appears healthy or not, should be treated as a potential source of infection. The prevalence of healthy throat carriers of *Str. pyogenes* has been recognized for a number of years, and their potential importance as a source of streptococcal infection of wounds was stressed during the early years of the recent war (e.g. Hare, 1940). The even greater prevalence of healthy carriers of *Staph. aureus* was recognized somewhat later, but it is by now well established that some 50% of normal people are nasal carriers at any one time; moreover *Staph. aureus*, unlike *Str. pyogenes*, is commonly present in small numbers on the skin of healthy people (Gillespie, Devenish & Cowan, 1939; Miles, Williams & Clayton-Cooper, 1944; Williams, 1946). There is evidence that the skin staphylococci are commonly derived from the patient's own nose. Thus carriage on the skin is more common in nasal carriers than in non-carriers; the skin and nose strains from one person are usually of the same bacteriophage type; and temporary elimination of staphylococci from the nose by the administration of penicillin is followed by their temporary disappearance from the skin (Moss, Squire & Topley, 1948).

Secondly, we may distinguish "infection of injury"—in which the bacteria are introduced into the wound at or soon after the moment of injury—from "added infection", in which the bacteria are introduced subsequently.

a. Self-Infection

It is evident that there are abundant opportunities for self-infection of wounds with staphylococci; the wounds observed by Williams & Miles (1949) were studied particularly to determine the extent to which this self-infection takes place. It may be said at once that the majority of cases of staphylococcal infection appeared to originate in this way.

The first point emerging from this bacteriological study was the great frequency of bacterial contamination of wounds at the time of injury: 18% of 393 trivial wounds swabbed within 20 minutes of injury yielded small numbers of *Staph. aureus*. It was possible to show that, in the majority of instances, these contaminants came from the patient's own skin. This early contamination apparently led to established infection and sepsis in a significant proportion of cases. Thus in small wounds treated by surgical trimming and suture and observed in a hospital out-patient department throughout their course, staphylococcal infection became established in the wounds of 72% of the 43 patients who, on the day of injury, had proved either to be skin carriers of *Staph. aureus* or to have their wound initially contaminated with the microbe, but in only 37% of the 428 who were not demonstrably carriers. Severe clinical sepsis developed in 30% of the patients with contaminated wound or skin, and in 16% of those with neither.

Further confirmatory evidence of the importance of self-infection was given by a comparison of the bacteriophage types of the staphylococci isolated from carrier sites, or from the fresh wound, with the type subsequently isolated from the infected wound. In 72% of 60 patients tested, the infecting strain was found to be the same as one of the strains isolated from carrier sites, or from the fresh wound, on the day of injury. The staphylococci producing sepsis seemed to be introduced into the wound at an early stage, since the sepsis was usually apparent on the first occasion that the wound was examined following the plenary treatment.

In general, it seemed likely that well over 50% of the cases of staphylococcal sepsis, developing in small industrial wounds treated soon after injury, resulted from infection with the patient's own staphylococci, and that these staphylococci were introduced into the wound at or soon after the time of injury. To what extent the remainder resulted from unrecognized self-infection, and to what extent from cross-infection, could not be determined.

The opportunities for self-infection with streptococci are clearly fewer than with staphylococci, since carriage, and particularly skin carriage, by healthy subjects is less common. In the group of wounds studied there was no clear evidence that more than a very small proportion of the streptococcal infections were derived from the patient himself, or were introduced at the time of injury.

b. Cross-Infection

The importance of cross-infection in wounds treated in hospitals received great emphasis during the war years, and much of the earlier work was reviewed by Miles in this Bulletin (1944). Briefly, study of war wounds in British hospitals from 1940 onwards showed that streptococcal infection was seldom an infection at the time of injury or a self-infection, but nearly always resulted from later added cross-infection in the hospital ward. These findings were amply confirmed in our study of small wounds (Williams & Miles, 1949) in which the few streptococcal infections occurred late in the wound's history and after the establishment of a staphylococcal infection; no source of self-infection was demonstrated.

The recognition of streptococcal cross-infection in wounds was made possible by the methods of type identification of streptococci devised by Griffith (1934); and the absence until recently of any comparable method for classifying strains of staphylococci delayed the clear demonstration that similar transmission of infection occurs in wounds infected solely with staphylococci (e.g. Rountree & Thomson, 1949).

Most of the more exact studies of cross-infection were carried out in hospital wards, but there is some evidence to justify an assumption that the situation is similar in factory surgeries. Thus Clayton-Cooper & Williams (1945) showed that in two factory surgeries, differing markedly in the rigour of the aseptic precautions adopted for the management of wounds, the more rigorous technique was associated with the lower over-all infection rate with *Staph. aureus*.

Summarizing, therefore, we may say that streptococcal infection of wounds is generally a late and added cross-infection ; the primary staphylococcal infection is commonly derived from the patient himself and seems to be introduced at or soon after injury, but secondary cross-infection with staphylococci also occurs.

c. Modes of Cross-Infection

It seems likely that in a factory surgery or a hospital out-patient department infected wounds form the most important source of cross-infection, although a heavy nasal carrier of streptococci may almost certainly be responsible on occasion. Just how important the healthy nasal carrier of *Staph. aureus* may be is not known, but in view of the frequency with which such carriers may contaminate their skin it seems likely that they should be regarded as potentially dangerous ; the question is one urgently needing investigation since some groups of workers, at least, have found that a great proportion of the staff of a hospital ward may be nasal carriers of penicillin-resistant staphylococci (Rountree & Thomson, 1949 ; Barber & Whitehead, 1949 ; Forbes, 1949).

In the same way as the infected wound is probably the most important source of cross-infecting bacteria, so contact seems likely to be the most important method of transfer to the new host. Contact may sometimes be direct, as when a nurse or doctor with a small infected lesion on a finger dresses a wound. But clearly infection by indirect contact must be far more common ; and the opportunities for it to occur are very numerous. Many of these opportunities are obvious : failure to sterilize instruments used in the dressing of the wounds between successive wounds ; failure to remove contamination from fingers that have come in contact with a wound ; failure to observe that a limb-rest may well become contaminated during the course of one dressing and that the contamination may then be transferred to the next patient's wound. Similarly, baths are always contaminated from any septic wound on a limb treated in them. As an example of more remote contact infection one may cite the contamination of sterile dressing material that may result from collecting material from the stock bowl or drum with instruments that have been used to dress a wound.

Contact infection, direct or indirect, is of importance whatever the size of the wound, and however long its dressing may take ; the risk of air-borne infection on the other hand is presumably roughly proportional to the area of the wound and the time during which it is exposed. The most important sources of air-borne infection of wounds are the various " secondary reservoirs " in the environment, such as bed-clothes, dressings (see, for example, Bourdillon & Colebrook, 1946), and floor dust ; and in factory surgeries or out-patient departments it is particularly the dust disseminated from dressings that is important. Other sources to be remembered are the nose and throat, and also the clothing, of medical attendants.

3. Prevention of Wound Infection

The adoption of the various improvements in aseptic technique suggested by McKissock, Wright & Miles (1941) has been shown on at least two occasions to be followed by a reduction in the incidence of streptococcal cross-infection (Logue & McKissock, 1945 ; Williams *et al.* 1945) ; and this, coupled with the fact that most streptococcal infections appear to result from cross-infection, suggests that it should be possible, by proper wound management, to prevent the occurrence of streptococcal infection of wounds under treatment. Moreover, the almost universal susceptibility of strains of *Str. pyogenes* to penicillin offers a ready method of treatment of wounds that are presented at the surgery with streptococcal infection already developed.

With staphylococcal infections the picture is complicated by the fact that in many, if not in most, cases the initial staphylococcal invasion of the wound is by microbes from the patient's own skin ; and by the presence of " endemic " strains of penicillin-resistant *Staph. aureus* in many hospital departments, and doubtless in factory surgeries also.

The management of a wound should therefore include, quite apart from the proper surgical treatment, measures (i) to remove any bacteria that already contaminate it at the time that it is first seen, (ii) to prevent subsequent self-infection from nearby skin, (iii) to prevent contact cross-infection during and after dressing, and (iv) to prevent air-borne infection during dressing.

i. *Removal of contaminants.* A number of trials have been made of various wound cleansing agents with the idea of removing bacteria as well as physical contaminants. Kerrigan (1942) reported on a very large series of wounds washed with soap and water, but provided no results from controls. Experience in Birmingham (see Williams & Miles, 1949) with the detergent cetyltrimethylammonium bromide (cetrimide), as well as with soap and normal saline, as wound cleansers, suggested that vigorous washing was of some value in reducing the incidence of wound infection, but that it was the vigour and extent of the cleansing rather than the nature of the cleanser that was the most important. Subsequently, Cruickshank & Squire (1949) reported a small number of cases of acquired sensitivity to cetrimide, and for this reason it may be desirable to substitute some other detergent for routine use in factory surgeries, where some men may have a number of small wounds treated at intervals. A sterile soap solution is an efficient detergent and may safely be used.

ii. *Prevention of self-infection.* For the prevention of self-infection after treatment two methods are available : the use of occlusive dressings and the use of persistent bactericidal drugs. In industrial practice occlusive dressings would have much in their favour quite apart from their contribution to the prevention of sepsis, as they would obviate the repeated re-dressing of wounds made necessary by physical soiling. With the development of cast nylon films (Bull, Squire & Topley, 1948), which are permeable to water-vapour but not to fluid water, satisfactory dressings that do not make the underlying skin " soggy " are becoming available and should prove of great value. The importance of an occlusive type of dressing in preventing wound infection of burns was stressed by Colebrook, Duncan & Butterfield (1947) and is particularly important in the case of wounds on parts of the body which are difficult to bandage, or on limbs that are in use.

The bactericidal drugs that have been tested on small

industrial wounds are the sulphonamides, flavines, and penicillin. Experience with minor lacerations and the like treated in hospital (Williams & Miles, 1949) showed that one single application of a sulphathiazole powder or cream, with or without added proflavine or penicillin, had no noteworthy effect on the incidence of sepsis. Repeated application, however, of proflavine-sulphathiazole powder, or of a lint dressing impregnated with the same mixture, did appear to reduce the incidence of sepsis in a small series of cuts seen and treated in a factory surgery.

iii. *Prevention of contact infection.* An early result of the investigation of casualties from Dunkirk and from the air-raids of 1940–41 on London was to draw attention to the potential risks of transfer of infection associated with the ward dressing techniques then commonly in use (see Medical Research Council War Memorandum No. 6, 1941, revised 1942, reprinted 1946). The Medical Research Council War Wounds Committee and the London Sector Pathologists planned a dressing routine designed to overcome these defects.

The first principle of this routine was the use of a " non-touch " technique for all manipulations involving the wound. It is impossible to insure sterility of the dresser's hands, but it is quite possible to carry out almost all the manipulations involved in a wound dressing with instruments, which can readily be sterilized by boiling in water for a short period. The use of sterile forceps should be a general practice whenever open wounds are dressed. Moreover, not only should the dresser's potentially infected skin be prevented from coming into contact with the wound or its immediate coverings, but it is also important that instruments that have been in contact with the wound should never be used to get material from the sterile stock, since this would lead to dangerous contamination.

To overcome the difficulties of maintaining an adequate supply of sterile material while forbidding the dresser to collect stock in the course of the dressing, the War Wounds Committee proposed the use of a dressing team, comprising a " dresser " who actually carried out the manipulations on the wound, a " trolley nurse " or " server " who was responsible for the supply of sterile material to the dresser, and a " runner " who helped to remove soiled dressings and who was generally responsible for the disposal of infected material. This general principle has, as was intended, been modified in many places to suit individual circumstances, but the plan of separating the functions of the dresser from those of the server is one that can be applied with profit in any dressing station where there is a rapid and continuous flow of patients. In factory surgeries a dressing team is commonly impracticable, but the single nurse working alone must observe the same basic rules regarding instruments and sterile stock : she should gather all the necessary dressing material before beginning a wound treatment, and if, after beginning, she needs further supplies, she must wash her hands and use fresh sterile instruments for collecting them. She should, of course, always wash and dry her hands between the treatment of successive wounds. Details of a routine suitable for a factory surgery were given by Williams (1944).

iv. *Prevention of air-borne infection.* As already mentioned, air-borne infection is of relatively minor importance as a risk to the small wounds treated in factory surgeries (though it is still a risk to bowls of sterile material left uncovered on dressing tables) but it cannot be completely neglected. All manipulations of soiled dressings should be reduced to a minimum, and bandages for removal should be cut rather than unwound, and should be put directly into a deep bin so that a minimum of infected dust is liberated from them. The floor should be washed frequently, or, if made of wood, treated with dust-laying oil. Where air-conditioned ventilation is employed, some adequate bacterial filter should be installed. In departments where larger wounds or burns are dealt with, more complex methods of air sterilization may be necessary (see Bourdillon & Colebrook, 1946).

4. Organization of the Factory Surgery

There is no doubt that a change from the less rigorous aseptic techniques that have been common in factory surgery practice to the more rigorous techniques indicated here demands an increase in the time spent on any individual wound treatment. It may be expected that this increase will be to some extent offset by a decrease in the number of cases of sepsis and a consequent decrease in the number of dressings required. Also, any method which enables the frequency of re-dressing to be reduced will lead to a saving of time as well as to a reduction in the opportunities for cross-infection that alone would justify the reduction.

However, there is one further method that may greatly contribute to a saving in the time spent on dressings, namely a reorganization of the lay-out of the surgery (Gissane, Miles & Williams, 1944). It may be taken as certain—though it appears often to have been forgotten—that no aseptic routine will be well maintained during the busy time in a factory if the lay-out of the surgery makes it difficult ; and a very real contribution to asepsis can be made by so arranging the equipment that the nurse has the minimum of walking between the basin where she washes her hands, the instrument sterilizer, and the dressing trolley.

5. Sepsis Developing in Untreated Wounds

The methods so far discussed are all concerned with the proper management of wounds after they are first seen in the factory surgery. But, of the cases of sepsis that are responsible for so much disability and loss of time in industry, only a small proportion result from infection occurring during treatment of the wound ; a far greater number develop in wounds so trivial that they are not noticed, or at least are not treated, at the time of injury (Williams & Capel, 1945). The prophylaxis of this sepsis is a very great problem, and probably lies to a large extent in the prevention of the trivial wounds that open the tissues to bacterial invasion. That is to say, it is an engineering and a psychological problem rather than a surgical or a bacteriological one. However, inasmuch as the staphylococci producing the sepsis probably come from the patient's own skin, there might be advantages in any method that would render the skin free from staphylococci, such as the use of medicated soap recommended by Fuller *et al.* (1948). Clearly, there is a need for much careful work before any method of this sort could be generally recommended, for it is most important that any such agent should be, as well as bactericidal, both non-irritant and non-sensitizing, even when used over very long periods of time. But it may be stated categorically that the prevention of all sepsis cannot be obtained by mere exhortation to the workers to attend the factory surgery with every wound, no matter how trivial, partly because many of the injuries that lead to

severe sepsis are so trivial as to escape notice, and partly because, without a great increase in staff, the surgery could not possibly deal with every trivial wound occurring in, for example, an engineering factory; besides which the attendance of all trivially injured workers at the surgery would lead to an intolerable loss of working time.

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THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH

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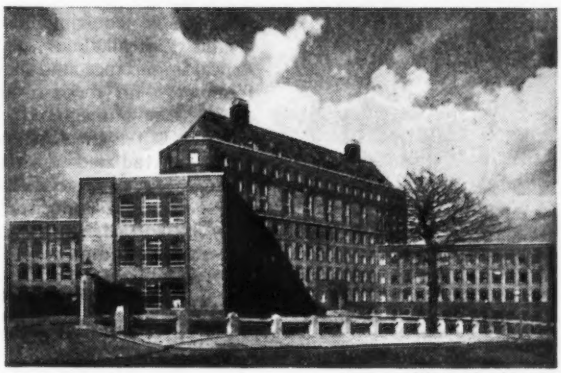
The recent transfer of the National Institute for Medical Research from Hampstead to the new and much larger premise t Mill Hill is an important landmark in the history of this institution; this therefore seems a suitable opportunity for a review of the current activities of the Institute, and an indication of the lines of expected development. The present article is intended to provide such a review. Some reference to the past history of the Institute must be made to provide a background, but as this aspect has been dealt with thoroughly elsewhere (Harington, *Proc. Roy. Soc.* B, 1949, **136**, 333) it will not be emphasized. Similarly, various descriptions of the building and its physical equipment have appeared recently, and these matters will be referred to only in so far as they are intimately related with the researches that are being discussed.

FIG. 1. GENERAL VIEW OF THE INSTITUTE



Westwood and Johnson

Early History and Development of the Institute

The decision to concentrate their efforts in laboratory medical research in a central institute was one of the earliest to be made by the original Medical Research Committee in the consideration of their general policy which they undertook on their appointment in 1913. The implementing of the decision was delayed by the 1914–18 war; nevertheless before this war broke out suitable premises at Hampstead had been secured and key members of the scientific staff appointed so that in 1920 a start could be made with actual research.

The work of the new Institute started in a modest way, with three main research departments, devoted respectively to physiology and pharmacology, experimental pathology and bacteriology, and applied physiology; there was also a Department of Statistics. At first each member of the scientific staff was personally responsible to the Secretary of the Medical Research Council; this arrangement was continued for some years until, with the growth of the Institute, it proved to be unworkable; it was ended in 1928 by the appointment of Dr H. H. (now Sir Henry) Dale as Director of the Institute.[1]

[1] See also: Green, F. H. K., "The Medical Research Council: its origins, constitution and functions," *Brit. med. Bull.* 1948, **5**, 352.

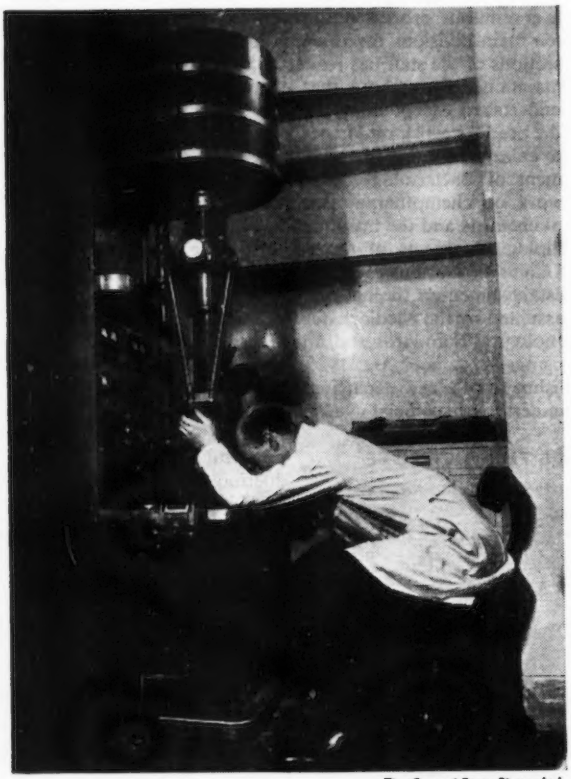
Extension of the range of work undertaken in the Institute began in the early years of its existence and has proved to be a continuous process until the present time when there are ten main divisions for research and the total number of all sections of the staff has reached 350. The principle has been maintained throughout that no major expansion should be undertaken except in response to a specific demand. Thus the need for work on viruses, which was early recognized, led to enlargement and broadening of the interests of the Department of Bacteriology; similarly the growing demand for work on chemotherapy necessitated strengthening the staff of chemists and the introduction of new workers to study the biological aspects of the subject. The acceptance by the League of Nations Health Organisation of the need for the establishment of Biological Standards, and the responsibilities assumed by the Medical Research Council in connexion with Biological Standards and under the provisions of the Therapeutic Substances Act, 1925, were the reasons for the establishment of a new department of the Institute which not only undertook the official work but itself became a centre of active research. Later, when the powerful impact of modern endocrinology on medicine made itself apparent a department for research in this subject was set up; and so the process of development has gone on.

Although mention has been made of the periodic establishment of new departments, this must not be taken to mean that the growth of the Institute has been by fits and starts; on the contrary it has been very gradual. What has been described as the setting up of a new department usually amounted in fact to little more than the appointment of one or two key members to the scientific staff and the provision of laboratory accommodation for them. Subsequent events have been determined by the course of the work, which in some cases has expanded along the lines originally envisaged and in others became redirected in the course of time; an instance of the latter is given by the history of the Department of Endocrinology, which in recent years has developed into the Division of Experimental Biology having much broader interests.

Furthermore, there has been another overriding principle, the importance of which cannot be too much emphasized. This is that there should be no rigidity in the organization which might lead to a sharp division between departments. On the contrary it has always been understood by members of the scientific staff that, whilst their primary duty is to pursue research in their own particular fields, they are no less under obligation to contribute to the general work of the Institute and particularly to help their colleagues with their specialized knowledge whenever such assistance is needed.

It was possible for some time to meet the demands for expansion raised by the increasing range of work by additions to the premises at Hampstead, together with the erection of ancillary buildings for special work, particularly on viruses,

FIG. 2. BIOPHYSICS DIVISION



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Focusing the electron microscope

on an estate which the Medical Research Council had purchased in 1921 at Mill Hill. By the middle nineteen-thirties, however, a limit had been reached to convenient expansion on the Hampstead site, and at the same time a further demand for a large extension of the work of the Institute arose. This was brought about by developments in chemotherapy and by the recognition by the Government of the need for increasing effort on this subject, which had always been one of the main lines of work pursued at the Institute. The Council therefore decided that proper provision for the future could be made only by the construction of a new and much larger building to house their central research establishment and they selected as the site for this building the estate at Mill Hill which was already in their possession.

The new building was started in 1937 in the anticipation that it would be ready for use in 1941. Once more the plans of the Medical Research Council for the National Institute were baulked by war, but after many delays and vicissitudes the task has finally been accomplished, and the staff of the Institute are now settled in their new home, which is certainly one of the finest and best equipped buildings designed for medical research in the world. The new Institute was officially opened by H.M. The King on 5 May 1950.

Research During the First Thirty Years

The present activities of the Institute, which it is the main purpose of this article to describe, are naturally in large measure the product of modern developments in medical research; however, in many cases they have their roots in the past, and at this stage it may therefore be worth recalling briefly the more outstanding achievements of the last thirty years. A prominent place among these is occupied by the physiological researches of Sir Henry Dale and his colleagues, chiefly on the chemical transmission of nervous impulses; this work led eventually to one of the great generalizations of physiology and won for Dale the Nobel prize for medicine in 1936. Again, the Institute can claim to be the original home of modern research on virus diseases; the identification of dog distemper as a virus disease and the discovery of a method for its prevention by Laidlaw and Dunkin, the isolation of the influenza virus by Laidlaw and Andrewes, the evidence for the virus theory of cancer provided by the work of Gye and Purdy and of Andrewes—all these are landmarks in the history of virus work and indeed in the development of medical research as a whole. The chemists at the Institute, led by the late H. W. Dudley and by Harold King, have made considerable contributions to chemotherapy and to the chemistry of alkaloids and other compounds of pharmacological importance, and they produced an idea which laid the foundation for modern steroid chemistry. A biochemical achievement of magnitude was the identification of calciferol (vitamin D_2) as the substance responsible for the antirachitic action of irradiated ergosterol; this was the first occasion on which a vitamin was obtained in the pure state. In the laboratories devoted to endocrinology, advances were made particularly in knowledge of the physiology of sex hormones and of the anterior pituitary gland. A wide reputation was also built up by the Optics Department, where the subject of ultraviolet microscopy was actively developed, particularly in relation to the application of the technique to work on viruses.

The result of the various major developments in the research work which have been mentioned was that when the time came for designing the new and larger Institute, many of the directions in which future expansion was desirable were clearly evident. What were not so obvious were the new developments which should be planned for, and in this connexion the enforced delay in completing the new Institute that was imposed by the war has not been without advantage. The most conspicuous example of this is afforded by biophysics, a subject which was scarcely recognized as part of the Institute's research programme before the war. Immediately before and during the war there was a rapid increase in the application of physical techniques to medical and biological research. To realize this one has only to think of the wide present-day employment of such methods as electrophoresis, electron microscopy, and, more recently, the use of isotopes as tracers. The temporary arrest of the project for the new Institute during the war allowed a pause for replanning, and this was used to make full provision for the future use of all physical techniques which had proved their usefulness. Furthermore the emergence of biochemistry as an independent branch of science and its manifold applications to medical research made it necessary to provide more space for this subject; in addition it was decided to include within the Institute the allied subject of bacterial chemistry, which

may be regarded from one point of view as the study of the basis of chemotherapy and in which so much progress had already been made by the Medical Research Council's Unit for Bacterial Chemistry under the direction of Sir Paul Fildes. It will be obvious that as the result of these additions the work of the Institute as a whole is on a very much broader basis now than could have been envisaged ten or fifteen years ago.

Present Activities of the Institute

Coming now to the actual activities of the Institute at the present time it is convenient to consider these under a few general headings; such headings will not necessarily be identical with the titles of the Divisions of the Institute since in many cases the general subjects of research overlap administrative boundaries, a process which is constantly encouraged. It will be noted for instance, that although the Biophysics Division is one of the largest in the Institute, the work of this Division will not be dealt with separately but will become apparent from what is said of other researches in which the members of the Division play an essential part.

Chemotherapy. Chemotherapeutic research in its broadest sense is one of the major activities of the Institute. The work falls into two main categories, chemical and biological. The chemical work comprises both conventional chemotherapeutic research consisting of the synthesis of series of compounds regarded on general grounds as likely to be effective in a particular disease, and also more subtle methods of attack such as the attempt to produce substances which may exercise chemotherapeutic activity by competitive interference with the essential metabolites of pathogenic micro-organisms. Apart from synthetic work a search for new antibiotics is maintained, although this is not on a large scale, the effort being concentrated on likely sources which may for one reason or another have escaped attention in the comprehensive surveys conducted elsewhere.

On the biological side an effort is made to maintain facilities for testing the action of new compounds both against typical pathogenic organisms, in vitro where this is feasible, and against a range of experimental infections in laboratory animals. Research is conducted on such questions as the precise mode of action of chemotherapeutic agents, and on the fundamental phenomenon of drug resistance, which is of practical importance. Closely allied to chemotherapy, and indeed perhaps lying at its basis, is research into bacterial chemistry; this is carried out on an extensive scale, the problems studied relating to the enzyme systems and the essential metabolites of bacteria.

So far as the diseases under investigation are concerned, there has always been and there still is a strong interest in tropical diseases; at the present time this is mainly directed towards filariasis and amoebiasis. Systematic research is being conducted on tuberculosis, in conjunction with the Council's Group for study of this disease. Finally, in co-operation with the Division of Virus Research, a constant watch is kept for the appearance of any new chemical compound active against virus infections.

Virus Research. Research on viruses, for many years a major interest at the Institute, continues to be one of the main features of the programme of work. The problem is attacked from many points of view. In the laboratories of the Division of Virus Research itself, intensive studies are being made of virus infections of animals, mainly those which cause respiratory disease. Within the division is included the World Influenza Centre, a laboratory administered by the Medical Research Council for the World Health Organization and directed by the Head of the Division. The function of this laboratory is to isolate and identify strains of influenza virus obtained from patients in the early stages of outbreaks of influenza arising in different parts of the world. The object is to study the epidemiology of influenza and the mode of spread of an epidemic, and particularly to maintain a watch for the appearance of aberrant strains of the virus which might have dangerous potentialities. Laboratory work on the common cold is also being conducted in this Division, and the Head of the Division is in scientific charge of the Common Cold Research Unit at the Harvard Hospital, Salisbury, which itself is an out-station of the Institute. Here, research into the common cold is carried out on human volunteers, and the range of investigation extends into field studies of the epidemiology of the disease.

The properties of viruses themselves, including bacteriophages, are constantly under investigation by physical and physico-chemical methods. Developments in electron microscopy are placing the study of the morphology of viruses on a new plane, and full use is made of the resources of the Division of Biophysics in this research. The earlier work of Elford, carried out in the Institute, on the approximate determination of the size of viruses by filtration through graded collodion membranes, is well known; recently, in the same laboratory, methods have been discovered for the rapid

FIG. 3. INTERNATIONAL STANDARDS DIVISION

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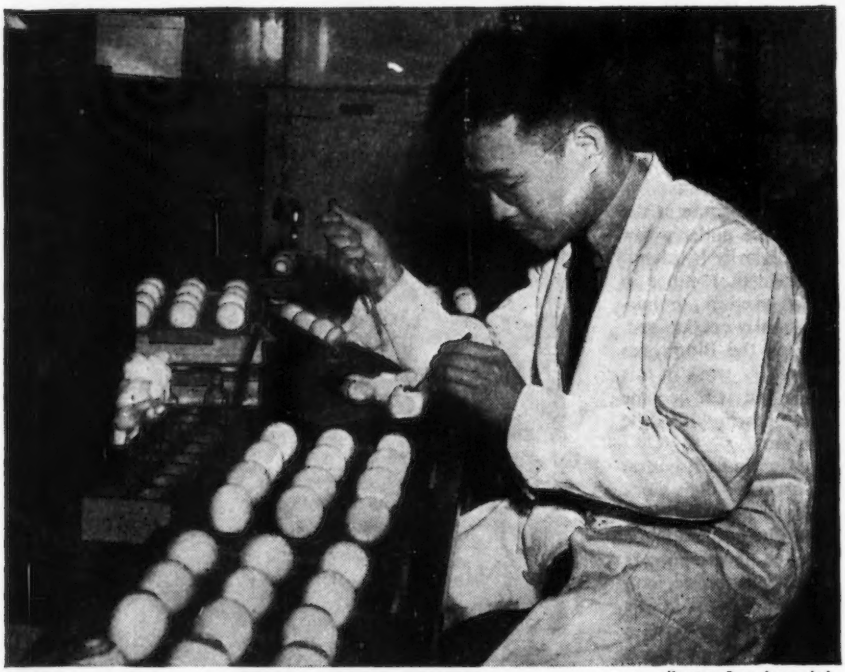
Distribution of material under sterile conditions

FIG. 4. VIRUS DIVISION, WORLD INFLUENZA CENTRE



Keystone Press Agency Ltd.

Harvesting influenza virus

isolation of viruses in the pure state by adsorption on laked avian red cells; this not only makes viruses much more easily available for physical and physico-chemical study, but it has led to the isolation of hitherto unrecognized forms of certain viruses which are of great interest.

Physiology and Pharmacology. The work carried out over many years by Sir Henry Dale and his colleagues on the transmission of the nervous impulse, to which reference has already been made, has been responsible for a general interest in chemical compounds which affect this process. One such compound is the chief active principle of curare, and a conspicuous advance was represented by the work of Harold King in the years immediately preceding the recent war, which led to the isolation and proof of the constitution of the highly active alkaloid *d*-tubocurarine. It was this work which made possible the development of the use of curare as an adjuvant in anaesthesia, and for the purpose of softening the convulsions in electro-shock therapy. Arising therefrom in the last year or two there has come a further development of importance in the discovery of the methonium series of drugs; these drugs, which are members of a homologous series of relatively simple compounds, namely straight-chain aliphatic substances carrying quaternary basic groups at both ends of the molecule, show a remarkable range of physiological action. Thus the compound containing ten carbon atoms—decamethonium iodide—is more active than *d*-tubocurarine in producing muscular relaxation, whilst those containing five and six carbon atoms antagonize the effect of decamethonium and themselves block the transmission of impulses through autonomic ganglia.

It is evident that these discoveries, apart from their important implications for practical medicine, open up a wide and fascinating field of pharmacological research, and this is being actively developed, with particular attention to the analysis of the mode of action of the compounds concerned. It is for instance already known that, although the over-all effect of decamethonium in producing muscular relaxation is superficially similar to that of curare, the mechanisms by which the effects are produced in the two cases are entirely different.

The work on the methonium drugs is only one of several activities of the Division of Physiology and Pharmacology, others being concerned with electrophysiological research and with the study of drugs that liberate histamine in the body.

General Biochemistry. The recent interests of the Division of General Biochemistry have been mostly in problems of biosynthesis and intermediary metabolism, and this seems likely to continue to be so for some time. Considerable light has been thrown on the mechanism of the biosynthesis of thyroxine in the last few years; work on this problem is still being pursued. In other researches great and increasing use is being made of isotopic labelling in the analysis of biosynthetic processes; thus sufficient information has now been gained about the biological precursors of porphyrin, and the way in which they are incorporated in the porphyrin molecule, to make it possible to construct a theory of the whole process of porphyrin synthesis which can be subjected to experimental verification. In the course of this work and of allied studies of porphyria unexpected facts have come to light concerning the normal and abnormal production of bile pigment. Similar methods are being applied to investigations of milk-fat formation, of methylation processes in the body and of mould metabolism. In all these researches the members of the staff of the Division of Biophysics have an important part to play. Under the general heading of biochemistry also come such researches as that which recently led to the isolation of the toxic substance from agenized flour, and work which is proceeding on the application of the methods of organic chemistry to the problem of protein structure.

Experimental Biology. As already indicated this division has grown out of the Department of Endocrinology. At present the main line of research is on problems of fertility. Arising out of a study of the preservation of spermatozoa, a matter of practical importance, an interesting line of work has developed which is being actively pursued. Surprising observations have been made on the retention of motility and, in occasional cases, of fertilizing power by spermatozoa which have been kept for long periods at low temperature in an

appropriate medium, with and without partial or almost complete removal of water. This opens up a new field of investigation and the work is being extended to the study of the effects of exposure to low temperature on the structure and metabolic processes not only of spermatozoa but of other cells. The research is being conducted in co-operation with the Optical Laboratory, with whose aid methods have been devised for the microscopical study of cells at low temperatures; these methods may well find a wider application in biological research.

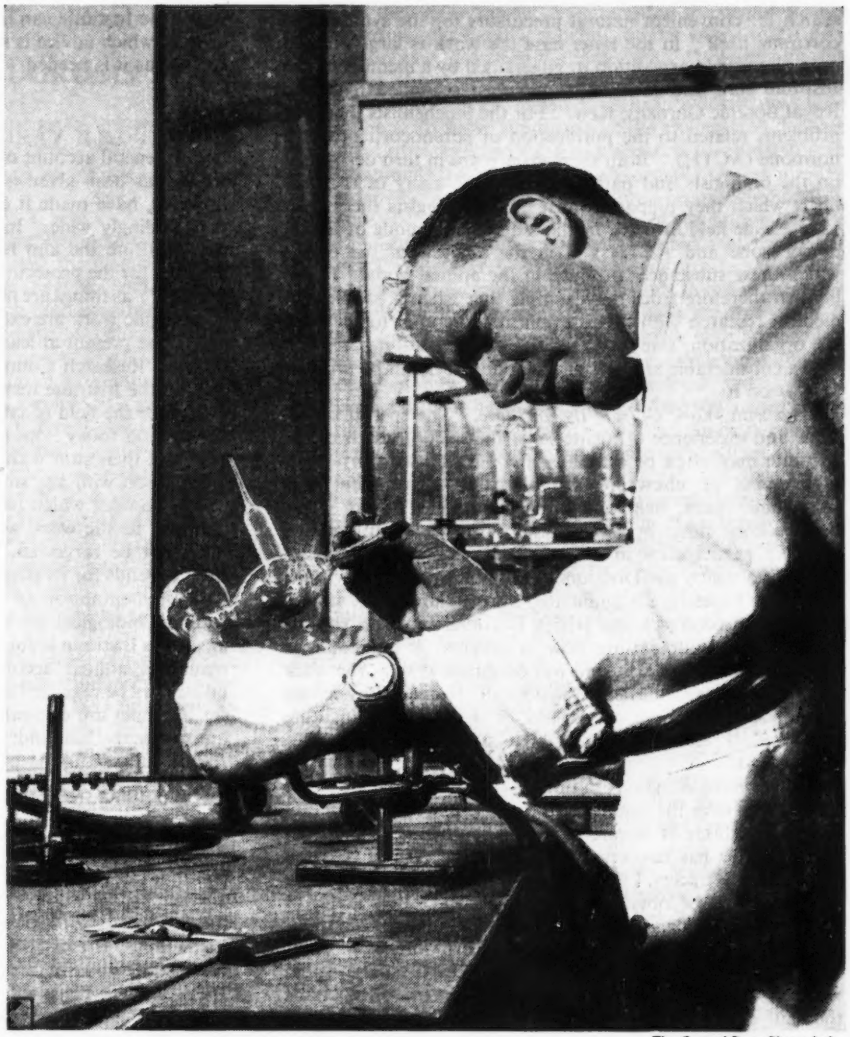
Biological Standards. The official work of the Division of Biological Standards has already been briefly mentioned. This work, which is now administered by the Council on behalf of the World Health Organization, consists in the establishment, maintenance, and issue of international standards for drugs, sera, hormones, vitamins and antibiotics whose potency must be assayed by biological as distinct from chemical methods; apart from its international work the Division has also advisory functions in connexion with the operation of the Therapeutic Substances Act. The advice of members of the Division is also sought on pharmacopoeial questions, both national and international. For the execution of this official work the Director of the Division of Biological Standards is able to call upon his colleagues in other divisions of the Institute for expert advice in their own fields. This method of operation avoids the necessity for a relatively large staff occupied for most of their time in routine work, and means that the opportunity for research enjoyed by members of the Standards Division is little less than that of workers in other laboratories.

The nature of the research work carried out in this Division will naturally depend on the interests of the Director. At present these interests are in bacteriology and immunology, and the main theme of current research is a comprehensive investigation of the mechanism of spread of local infection and of the factors affecting this process.

Special Researches. It is, or ought to be, an advantage of a large research institute, that when the need for special research on a subject with many different aspects arises unexpectedly, members of the staff having relevant expert knowledge are available to turn their attention to the new problem. So far as the Institute is concerned this was of course illustrated during the war, when groups of workers combined to study such urgent practical matters as air hygiene, physiological problems affecting submarine operations, methods of protection against flame-thrower attack and so on.

A peace-time situation of a similar sort has recently arisen in connexion with research on cortisone and adrenocorticotrophic hormone. Laboratory investigation of this problem as a whole involves organic chemists, biochemists, experimental biologists and pathologists. Men skilled in all these branches of science are available on the staff of the Institute and accordingly research has been undertaken on various aspects of the general problem, which involves work in and close co-operation between several of the divisions of the

FIG. 5. CHEMISTRY DIVISION



The Central Press Photos Ltd.

Glass-blowing

Institute. Thus the chemists are working on the synthesis of compounds analogous in structure to cortisone and on the search for convenient natural precursors for the synthesis of cortisone itself; in the latter case the work is largely based on a recent field expedition to Nigeria led by a member of the Institute staff and including a botanist seconded from the Royal Botanic Gardens, Kew. For the biochemists there are problems related to the purification of adrenocorticotrophic hormone (ACTH). Both these groups are in turn dependent on the biologists and pathologists for the assay of the products which they prepare, whilst the pathologists themselves have a wide field of work in the study of the mode of action of cortisone and ACTH and in the analysis of the effects which these substances produce in the animal body. It will be seen therefore from this example that when a problem of medical research with broad implications comes to the fore, the organization, staff and facilities of the Institute are such that a considerable amount of scientific effort can be brought to bear on it.

Help with Work Outside the Institute. The special knowledge and experience of members of the scientific staff of the Institute may often be of value in connexion with investigations going on elsewhere. In all cases where there is a reasonable claim, help and advice are freely given. This may be done either by service on appropriate committees or by actual participation in the work. An example of the latter is the help which the Division of Physiology is giving, based largely on experience accumulated during the war, in studies of decompression sickness arising in connexion with various large tunnelling operations now in progress in this country. Further instances of this kind will doubtless arise as the work of the newly established Division of Human Physiology develops; this division forms part of the National Institute for Medical Research although it is actually housed at Hampstead.

Furthermore, it may from time to time fall to the lot of the Institute to take the initiative in helping to provide facilities for new methods of research involving special technical difficulties. This has happened recently in the case of research with isotopic tracers. In the early stages, when supplies of isotopes could be obtained only from the United States of America, the Medical Research Council assumed the responsibility of receiving the material and distributing it to other laboratories where it was required for research. The actual work in this connexion was undertaken by the members of the staff of the Division of Biophysics, who also combined with the Telecommunications Research Establishment in the design of suitable equipment for assay. A mass spectrometer was constructed in the Institute with which analyses have been and are still being carried out not only for members of the Medical Research Council's staff but for many other medical and biological research workers engaged in experiments involving the use of stable isotopes. In the natural course of events, laboratories working with isotopes, as they gain experience, are becoming independent of help of the kind which the Institute can offer. Even now, however, cases still arise in which advice is sought, and such advice will be given so long as it is needed.

Conclusion

The general account of the present activities of the Institute which has been given is in no way comprehensive. It will, however, have made it clear that the range of work covered is exceedingly wide. In the design and organization of the new Institute the aim has indeed been to provide staff and facilities for the prosecution of any kind of laboratory medical research; as things are nowadays this means that few branches of scientific work are excluded.

For the present at least this object has been achieved. The Medical Research Council have appointed to their scientific staff in the Institute men and women whose combined interests cover the field of laboratory research in medicine as it is understood today; moreover in the new building they have provided their staff with space and facilities which will stand comparison with any similar institution in the world.

The account which has been given in this article has been confined to the work which is done in the laboratories; it must not be forgotten, however, that the laboratory work itself depends for its efficiency on general service departments. Of supreme importance among these, in an institution where so much biological work is done, is the animal house. Here again the Institute is fortunate in the provision that has been made for animal accommodation. Moreover, the animal house may be regarded as itself in part a research department, for attempts are constantly being made to discover ways of improving the husbandry of experimental animals. Mention should also be made of the extensive provision within the Institute for the design and construction of special instruments.

How long the aim for completeness, which those responsible for the design of the new Institute have kept in mind, will continue to be fulfilled is a question which only time can answer. Reflection on the development of biophysics within the last few years shows how rash it would be to attempt a prediction. It can be assumed that the general lines of investigation now in progress will continue to be pursued. Work in some fields will doubtless expand; in others it may diminish. The secure position that has now been won for medical research makes it certain, however, that the over-all effort will show steady growth, and in this growth members of the staff of the Institute will be encouraged, by their fortunate environment, to assist. It may therefore be hoped with reasonable confidence that the Institute, in its new quarters, will continue, as in the past, to exercise a beneficial influence on the progress of medicine.

INDUSTRIAL FLUOROSIS

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A characteristic property of fluorine compounds is their ability to act as a flux, that is, to assist the fusion of other compounds with which they are heated. Accordingly, minerals containing fluorine are much used in industrial processes. Examples are the use of fluorspar (calcium fluoride) in the manufacture of iron and steel and of cryolite (sodium aluminium fluoride) in the preparation of aluminium. Fluorine and its compounds are toxic when inspired or ingested and, since they may be encountered in different ways in many industrial processes, they present a definite hazard to health. Fluorosis in man and animals from industrial causes has been known for many years and has occurred in many countries. Animal fluorosis in the vicinity of factories discharging fluorine-containing gases, fumes, or smokes is due to the consumption of pasture on which fluorine compounds have been deposited. Weather conditions, such as the persistence of the prevailing wind and the amount of rainfall, are important.

When Roholm (1937) published his classical monograph, *Fluorine intoxication*, it attracted little attention in this country and, although serious consideration could have predicted the occurrence of fluorosis at Fort William, it was not until 1944 that any investigation was initiated. Human fluorosis of man's own making has occurred in factories making or using hydrofluoric acid, in the mining of fluorine-containing ores, in the crushing of these, and in industrial processes which use them. Wilkie (1940) recognized osteosclerosis radiologically in two Yorkshire workmen occupied in the manufacture of hydrofluoric acid and of aluminium fluoride. Subsequent analyses showed that their daily urinary output of fluorine was at least four times that of normal controls. Twenty-eight industries which use either fluorine compounds or materials in which fluorine is present as an impurity are listed in Sappington's *Essentials of industrial health* (1943). To this list must now be added industrial concerns which use phosphatic iron ores of a relatively high fluorine content or coals containing fluorine. The increasing industrial use of compounds of beryllium and fluorine has led to the existence of the hazards of non-occupational neighbourhood poisoning, which presents a challenge not only to the guardians of health in industry, but to public health authorities in industrial communities generally.

The first outbreak of animal fluorosis in cattle reported in Great Britain occurred in 1941 in the vicinity of brickworks in Bedfordshire, resulting from the burning of fluorine-bearing marine clay. The general symptoms of chronic fluorosis in both man and animals have been noted in cases of endemic and industrial fluorosis and have also been produced experimentally in animals. Dental changes in young persons and animals, and bone changes, always occur when more fluorine is assimilated than can be excreted.

Dental fluorosis is recognized by the appearance of the teeth where fluorine poisoning has taken place during the period of their development. On eruption the dental enamel shows opaque chalk-white patches, or the whole tooth may have an opaque, dead-white appearance. Subsequently, the tooth may show an orange-yellow pigmentation which becomes brown or black. Where fluorine intoxication has been severe, the teeth show hypoplasia of the enamel and dentine, they are brittle and have a low resistance to abrasion. In grazing animals the teeth become abnormally worn and often broken, so that mastication of hard foods becomes impossible. Exposure of the tooth pulp and trauma of the gums have been found. Animals in this condition show signs of pain when they drink cold water.

Fluorine is an accumulative poison and, stored in the body, is deposited in the bones and teeth, with the formation of fluorapatite. The bones become enlarged, with the production of exostoses, and ultimately the whole skeleton is affected. Radiograms show calcification of ligaments and a greatly increased density of bone, particularly of the cancellous bones. The bones are brittle and readily fracture. In man, owing to the strain and stress of erect posture, the vertebral column and pelvis are early and most severely affected, with progressive rigidity of the spine and neck, accompanied by pains.

Roholm made a detailed investigation of fluorosis amongst cryolite workers in an aluminium factory at Copenhagen. Their chief symptoms were gastritis, rheumatic pains, stiffness and finally rigidity of the spine, immobility of the ribs and interference with breathing. On *x*-ray examination the bones showed increased density, osteosclerosis and marked exostosis (Roholm, 1937).

In animals, urinary analysis can reveal incipient fluorosis and is now an established procedure. The urinary levels of fluorine depend on the amount ingested and the time the animal has been at risk. High values are associated with bone lesions, which give rise to lameness and crippling. Animals appear to suffer extreme joint pain, so that movement is stiff and laboured, grazing becomes difficult and the animals tend, therefore, to inanition. With less severe bone lesions, removal to uncontaminated pastures leads to recovery, though a high level of fluorine may persist in the urine for some considerable time because of the elimination of fluorine stored in the skeletal system.

Symptoms of fluorine intoxication in animals also include reduced rates of growth in young animals and loss of weight, sometimes accompanied by loss of appetite; in older ones, lactation is reduced and there is thirst and coarsening of the coat.

Fort William

Attention was drawn to the escape of fumes from the aluminium factory at Fort William when a crofter complained that an unknown disease was attacking his sheep (see Medical Research Council Memorandum No. 22, *Industrial fluorosis*[1]). Investigation showed that the sheep, and also two cows, all of which grazed in the path of the smoke-cloud, were suffering from fluorosis. Later on, the condition was found to exist on other neighbouring farms where animals grazed within two miles of the factory. Dental lesions were seen in all the affected animals bred on these farms. Affected cattle and sheep also exhibited wasting, harsh, staring coats,

[1] For particulars, see p. 122.

reduced milk-yield and bone disorders. Post-mortem bone examination showed that the elasticity, measured by finding the breaking-strength, was much below normal. The radius and ulna of one sheep were found to contain 10,300 p.p.m. fluorine. The radius and ulna of a control sheep contained 279 p.p.m. fluorine.

At Fort William, aluminium is produced by the electrolytic decomposition of alumina in molten cryolite. In this process, volatile fluorine compounds and cryolite-contaminated dust are emitted. Factories built for the manufacture of aluminium by this method are generally situated near to a source of water-power. This fact renders the degree of neighbourhood fluorosis less serious than it might be elsewhere, as the population of mountainous districts is sparse and scattered and the number of farm animals is small. In the surrounding area, fluorine compounds will be found deposited on the outer surface of leaves and on the stems of plants.

The factory at Fort William in the Western Highlands of Scotland is situated at the junction of four valleys, the largest of which is Glenmore. (The smaller factory at Kinlochleven, nine miles to the south, is surrounded on three sides by hills and has Loch Leven on the fourth side.) The prevailing wind is south-south-west. At the time of the investigation, the fumes were not " scrubbed " or treated in any way and a dense white cloud drifted over the countryside. Fort William has one of the highest rainfalls in Great Britain. Rain, while reducing the persistence of a smoke cloud, would assist leaching of soluble fluorides deposited on the surface of the soil.

The investigators classified the Fort William population into three groups according to degree of exposure to fluorine. The operators in the furnace rooms were considered to be the most exposed (Group I). Into the second category came factory employees not engaged in the furnace rooms (Group II). Lastly, there were villagers not employed by the aluminium company and living at least a quarter of a mile from the works. The first group was subdivided because the three furnace rooms differed from one another in several respects. Furnace Room A, the oldest one, lacked artificial ventilation and was very hot and dusty. Furnace Room C, the newest, had an adequate draught system drawing away the fumes from the furnaces directly and was free from dust. Furnace Room B was intermediate in type between A and C.

Clinical Findings at Fort William

At the time of the clinical investigation, the employees comprised 668 men and 114 women.

Digestive disturbances were reported by 14.7% of the persons in Group I, by 10.1% of Group II and by 5.2% of Group III. These complaints were mostly of dyspeptic symptoms and occasional attacks of indigestion. There was very little evidence of abnormal physical signs. The results of toe-touching tests for spinal rigidity were rejected in view of the radiological findings. Certain of the *x*-ray films revealed abnormalities in some of the older furnace men who had been exposed to fumes for many years. Abnormal radiograms were seen in 25.4% of Group I, in 8.3% of Group II and in 4% of Group III. All the schoolchildren examined appeared to be normal. In affected persons the abnormality tended to be in the tibia and fibula. Small irregularities were present at the medial border of the tibia, with sharp upper and lower margins and sometimes bearing small spicules.

Blood fluoride analysis gave varying results that did not coincide with the positions of the subjects in Groups I, II and III. Haemoglobin estimations and blood-cell counts, taken collectively, showed no abnormality in any of the groups. Fluorine determinations carried out on urine samples showed that male subjects in Group I excreted about 8 mg. of fluoride per 24 hours, those in Group II excreted about 1.5 mg. and those in Group III about 0.8 mg. The corresponding figure for the schoolchildren was 0.4 mg. per 24 hours.

In a dental examination of 373 children, 21 were found to have mottled teeth. In no case was the mottling severe and usually it was very slight.

The conclusions drawn were that in the factory the workers in the old furnace room inhaled considerable quantities of fluorine and, judged from the urinary excretion, also absorbed considerable quantities. Although bone changes, demonstrable by *x*-ray examination, were seen in a proportion of these workers, none of them suffered clinical disability attributable to these changes. It was considered that some of the workers were exposed to a definite risk and that the conditions within the older type of furnace room were such as to call for determined efforts to reduce the degree of exposure to fluorine.

There was less certainty about the risk to human health outside the factory. Clinical examination of a small number of residents in the neighbourhood had shown no signs of injury to health, but it was pointed out that it would be prudent to site new developments in such a way that, so far as possible, residents are kept out of the zone known to be most liable to contamination. This investigation has at least drawn attention to the possibility of fluorosis arising in human beings in the neighbourhood of industrial undertakings emitting fluorine-containing fumes and dusts.

It is therefore gratifying to know that the danger of fluorine has been recognized by the extension of the manufacturing processes controlled under the Alkali, etc. Works Regulation Act, 1906 to include volatile organic sulphur compounds and fluorine on the list of noxious or offensive gases, the discharge of which into the atmosphere is controlled; but, until this control becomes really effective, and the number of likely sources of fluorine is known, we have no evidence of the extent of the occurrence of neighbourhood fluorosis.

Neighbourhood Fluorosis

The recognition of fluorosis in farm animals in Lincolnshire, where open calcining of iron ore containing 1,200 p.p.m. of fluorine with coal containing 100 p.p.m. was carried out, led to a pilot investigation into the possibility of a human hazard. The human population in the affected area consisted of the occupants of one farm, each of whom complained of one of the following symptoms: stiff joints or back, gastric trouble, or cough, symptoms which, taken into consideration with the fact that the window glass of the farm house was etched by the fumes from the burning ore, are indicative of fluorine intoxication. Fluorine is also added as a flux in the manufacture of steel, and the occurrence of outbreaks of an animal fluorosis is of increasing frequency and in several areas has been associated with the etching of window glass. This means that the human population is also exposed to a hazard, the magnitude of which is difficult to assess because man is less vulnerable than grazing animals. It was suggested by Murray & Wilson (1946) that neighbourhood fluorosis should

receive serious consideration in view of the recent extension of the iron and steel industry.

In towns or in their outskirts, where there is a concentration of factories, power-stations, and gasworks, all or some of which may be emitting fluorine-containing gases, smokes or dusts, the absence of grazing animals may deprive us of what has hitherto been the only means of recognizing the existence of a source of danger. Several cases of marked dental fluorosis have been seen in persons born or bred in the eastern districts of London, where there is a great concentration of industrial undertakings.

It must, however, be emphasized that dental fluorosis, the characteristic white mottling of the dental enamel with or without brown staining, can occur only when the teeth are subjected to fluorine during their development. Therefore dental fluorosis should not be used as a sign of industrial fluorosis within a factory and only with reservation as a sign of neighbourhood fluorosis.

Though we are not here concerned with endemic fluorosis, the fact that fluorine holds a peculiar position with regard to its effect on man by reason of its power at low levels of ingestion to protect against the incidence of dental caries, yet at higher levels to cause marked skeletal abnormalities (Shortt *et al.* 1937; Ockerse, 1941), makes the subject of fluorosis a matter of much controversy. Fluorine compounds have been used as a tool by biochemists as an enzyme poison and this fact should give a clue as to its mode of action. It cannot be over-emphasized that what is really wanted is some means of recognizing the early signs of excessive fluorine intake in man, or some agreed level of intake which can be tolerated over many years without harmful effects. Radiological examination of the bones does not appear to be suitable for this purpose and so some other criterion must be used. McClure *et al.* (1945), as a result of human balance experiments, established that up to 5 mg. of fluorine can be ingested and eliminated per day, and that with a greater intake there is retention, which we know from past experience will lead to its accumulation in the bones and hence produce the characteristic bone changes, possibly only after 20 years' exposure.

It has previously been suggested that a test based on the daily urinary excretion could be used to establish the level of fluorine intake. In this one must take into consideration the natural sources of fluorine, which are principally water, tea, and fish products. A practical point to bear in mind is that an increase of dietary calcium decreases the toxicity of ingested soluble fluorine compounds, presumably by decreasing fluorine absorption, calcium fluoride being relatively insoluble, and therefore milk consumption should be encouraged in all persons exposed to a fluorine hazard. In this problem of fluorosis, as in all others which involve a health risk, we must aim at prevention. Hence, the extension of the Alkali Act to include fluorine is timely, particularly in view of the fact that the use of fluorine compounds, through the extension of existing industries and the introduction of new undertakings, has increased by leaps and bounds in recent years.

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EYES IN INDUSTRY

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For one reason or another, the subject of vision has in recent times hardly received from physiologists the attention which it deserves. Sight is rightly regarded as the queen of the senses, and as a science it provides an attractive array of complex, unsolved mysteries; yet, for the most part, physiologists have passed it by for what they presumably regard as more profitable fields of study. On the clinical side, ophthalmologists have, of course, been very active, but the scientific study of vision has been left very largely in the hands of physicists and illuminating engineers.

Recent evidence for this is Mr H. C. Weston's book, *Sight, light and efficiency*.[1] Mr Weston has been responsible for a number of fundamental researches on vision, in which he has been particularly concerned to discover the factors which limit the performance of visual tasks under given conditions. He has, as it were, dissected various tasks to discover the critical detail which has to be resolved and to determine the relative importance of size, contrast, colour, illumination level and so on.

There is an inherent danger in becoming too introspective about how and what we see. Seeing is such an everyday affair that we do, and should, take it for granted; once we start to think about the constituent elements in the visual image and are no longer aware simply of an integrated perceptual pattern, our interpretation of what we see becomes less instinctive and our reaction less automatic. Hence, while the visual expert may legitimately proceed with his analysis, it is no part of his business to dissect the task in front of the observer's eyes. His aim, on the contrary, must be to control the visual situation by appropriate design of the lighting, by the choice of background, by the design and colouring of the objects in the field of view, so that perception and recognition are made as easy as possible. In this way the work of an operator in a factory is simplified, and there is consequently less eyestrain, less bodily fatigue, a happier mental outlook, greater efficiency and higher output.

This goal is the theme of Mr Weston's book—a most satisfying theme too, since it should commend itself to both management and workers alike.

The Problems Analyzed

In any particular industrial operation, the problem of vision and lighting may be subdivided into four parts: (i) the analysis of the visual task, (ii) the determination of the optimum type of lighting and the best arrangement of the parts that have to be manipulated, (iii) the selection, if required, of operators with vision suitable for the task, and (iv) the provision of visual aids where appropriate. Stated in this way, the procedure appears to be fairly straightforward, but each stage has its own peculiar difficulties. In the analysis of the tasks, for example, the question of fine detail has to be considered in relation to the resolving power of the eye, differences of colour and brightness in terms of visual discriminating capacity, differences of distance in relation to stereoscopic acuity, and the like. As Weston shows, even the simple task of threading a needle has all these aspects and is itself quite a difficult task to analyze.

Once the nature of the primary visual observation has been determined, the type and level of illumination required can be specified in general terms, although each task must to some extent be considered as an individual problem. A considerable amount of data, much of it derived from Weston's own experiments, is available on the illumination levels appropriate for each object in relation to its size, the contrast afforded by the background, etc. The question of directional or diffuse illumination, or some mixture of the two, has to be settled, depending on whether, for example, shadows are a help or a hindrance, and on whether it is desirable to enhance the three-dimensional appearance of the scene. Provision of a light background may help to outline the dark parts of a machine, while the pattern and lighting immediately surrounding the work may be designed to provide lines which tend to direct the eyes to the functional part of the machine, much as a cathedral spire lifts the eyes to Heaven.

We must note here, however, a potential conflict of ideas. On the one hand, we have the school of thought which, by means of devices such as those just mentioned, advocates the maximum possible concentration of the operator's attention on his task, and the removal of all external distractions. On the other hand, prolonged concentration is in fact impossible, and surely undesirable. From time to time the operator must be encouraged to look around to give his eyes some relief, and if no natural vista is available to him, then even a picture on a wall may be a desirable substitute.

Thus, in a report, *Researches on the measurement of human performance* (His Majesty's Stationery Office, London, 1950), published by the Medical Research Council, it is shown that, after half-an-hour, measurable deterioration will occur in the efficiency of an observer in a task requiring concentrated visual attention, and that something in the nature of a rota of occupations may be desirable to maintain maximum efficiency. To translate this suggestion to the industrial field may be impracticable, but at least we have here an obvious warning against any excessive concentration on the work. It should in fairness be emphasized that Weston does not err in this way; on the contrary, he strongly advocates the well-lit and almost gaily decorated factory which can provide just the change of scene for the operator whose work is normally located quite near to him.

The next stage concerns the selection of the operator. Eyes differ and observers differ, and even when preliminary training has been given, it may be found that some persons are less suitable and less efficient at a particular task than others. Poor visual acuity may be the cause, or a greater tendency to visual fatigue, or less sensitivity to movement. Whatever the reason, it is eminently desirable both for the happiness of the worker and the efficiency of production that in such a case some screening of the operators should be attempted. The most striking example of this is in operations requiring good colour vision, where workers with defective colour vision are

[1] For particulars, see p. 122.

likely to be at a permanent disadvantage. This question was discussed at length in a *Report on defective colour vision in industry* published in London in 1946 by the Physical Society, and a strong case was made for pre-vocational testing of colour vision and also for testing in schools. In certain occupations a worker with defective colour vision in the wrong job may not only be inefficient, but may lose the chance of promotion which he would otherwise have earned, and there are also industries where failure to recognize a colour signal correctly would be a serious source of danger. Thus, one oil refinery was quoted where colour defectives were definitely barred.

This raises the question of the rather widespread use of colour codes to distinguish the various services in a factory and their use sometimes to mark the danger points. Unfortunately, reds, oranges, browns and greens are among the colours frequently confused by the colour defective; yet a colour code would be severely restricted if these colours were avoided. To make matters worse, blues and greens tend to be confused by normal persons when the light is poor or the object small. It follows that colour coding must be applied with caution and, wherever possible, distinctions of pattern should supplement distinctions of colour.

Mr Weston makes some interesting remarks on vocational sight-testing and points out that in general the tests are relatively simple to employ. He does not shrink from advocating that, where the number of oculists or ophthalmic opticians is inadequate, the tests might be undertaken by lay operators. No doubt objections can be raised to this suggestion, but if the alternative were to omit the tests because of a shortage of visual specialists, the proposal would surely be worth a trial.

While the need for a high degree of illumination in fine work is by now widely recognized, it is less generally realized that, relatively, a much greater advantage is achieved by using an optical aid to increase the apparent size of the detail. Thus a simple magnifying lens giving an enlargement of only 2 may be equivalent, from the point of view of resolution of detail, to an increase in illumination of perhaps 5 or 10 times. In view of this, a much wider use of optical aids in industry might have been expected, but in many cases their inconvenience is too great a deterrent. One of the most useful aids is the binocular magnifier, worn as a pair of spectacles but differing from ordinary glasses in that each glass has a lens and a prism action. This has the advantage that both accommodation and convergence are relieved in very near work and much eyestrain can be avoided. Weston argues most convincingly for their more extended use, but there is great reluctance on the part of the workers to wear them.

The case for what Weston describes as " incentive luminance and colour " is probably as strong as for any other aspect of good lighting, but the argument must have a psychological rather than a visual basis. The effect of working in a well-lit factory with walls, floor, machines, etc. decorated in light and attractive colours can be felt rather than measured. While some managements may have doubts on the score of expense, the more enlightened firms see its justification in the improvement in the morale of the workers, in a greater pride in the cleanliness of the machines, in a smaller labour turnover, and, as Weston aptly puts it, in its contribution to dissociating " irk from work ".

Prevention of Accidents

One very important purpose in planning and decorating a factory is the prevention of accidents. Dark machines operating in a dark environment are a much greater potential danger than similar machines operating in a good light. It will not do, of course, for everything to be too light, since a machine or an obstruction will be seen best when there is a good contrast between it and its background. Nevertheless, the possibility of achieving a good contrast exists only when the degree of illumination is high, as experience of the black-out brought home very forcibly. It must also be remembered that the eye responds more rapidly at high degrees of illumination.

In addition to the prevention of general bodily injuries there is the problem of injuries to the eye itself. It is clear from a table given by Weston that eye hazards are much greater in some industries than others. Flying particles are responsible for a great many accidents though in some occupations the wearing of protective goggles would no doubt be rather inconvenient. Nevertheless, a wide variety of goggles, giving protection against both particles and harmful radiations, is now available, and there seems little doubt that the many injuries which do occur each year could be greatly reduced in number if it were not for individual negligence in taking reasonable precautions. How to eradicate negligence is a problem much wider than that of vision alone.

There are many people who can contribute to the better lighting of our factories, although it is by no means clear who should have the main responsibility. It is a specialized task, yet illuminating engineers, oculists, ophthalmic opticians, artists, architects, physicists, may each consider that their training should be the basic training. Perhaps, in due course, a hybrid individual may emerge, to some extent a Jack-of-all-trades who is yet master of this complex art; indeed, Weston's book provides the best possible foundation for this new career of occupational optics.

OPERATIVE OBSTETRICS[1]

A Book Review

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The fifth edition of this standard work has been awaited with the greatest eagerness by " obstetric specialists or prospective specialists " and " general practitioners who are seriously interested and actively engaged in obstetric practice." It is for them that the book has been " primarily " written. The quotations are from the preface, for which Emeritus Professor Munro Kerr has accepted responsibility.

First published in 1908, this famous textbook appeared in its fourth edition in 1937. During the weary years of tumult between the appearance of the fourth and fifth editions the art and science of obstetrics has shared in the general upheaval. When the fourth edition appeared the treatment of puerperal sepsis with sulphonamide drugs was in its infancy, and escaped notice in the book's index. Blood transfusion was still regarded as rather unusual. The use of radiology in obstetrics was a comparative innovation. The extent to which obstetrics has advanced may be measured by a brief consideration of the above facts, and in the circumstances it is not surprising to find that the size of the volume has increased from 832 pages in 1937 to 934 in 1950, both figures exclusive of the index. Indeed, in the circumstances, it is very much to the credit of the authors that the increase has been restricted to a mere hundred or so pages. The introductory chapters on the management of normal labour (Part I in the new edition) remain virtually the same in length. Part II (" Dystocia due to faults in the forces ") is increased by eight pages. Part III (" Dystocia from faults in the foetus ") is awarded an additional 11 pages, Part IV (" Dystocia from faults in the parturient canal ") exceeds by four pages the space devoted in the 1937 edition, while Part V (" Obstetric operations ") has 368 pages, six more than allotted in the fourth edition. Part VI (" Injuries and accidents to mother and child "), in its 112 pages, is allotted no less than 52 pages more than in the previous edition. This is chiefly accounted for by an additional chapter " A review of the factors influencing maternal mortality, stillbirths and neo-natal death " which has no direct counterpart in the 1937 edition. This admirable chapter is the work of C. Scott Russell.

It will be noted from the above summary that the title of " Operative obstetrics " remains, as in the previous editions, rather misleading. The sub-title, " A guide to the difficulties and complications of obstetric practice", is much more informative. We are not dealing here with a mere textbook of surgical midwifery, but with a guide, friendly and philosophical, to the difficulties. Indeed it is the philosophy and friendship which pervade the book that make it so charming. This quality, akin to good conversation after dinner, it possessed in abundance in its previous editions. It has been caught admirably in this one, to be imprisoned in small print interjections, in which the authors reveal by the use of their initials their individual and not always identical views. Pithy anecdote, vivid phrase, and that peculiarly Scottish brand of humour described as " pawky " are not wanting in these asides, which give the book an added value.

The illustrations are many and varied. The well-tried line drawings of A. K. Maxwell and D. J. Kidd predominate, but there are a large number of new photographic illustrations. Of these, the reproductions of *x*-ray films are particularly numerous and well chosen. Many of them have already appeared in print (by courtesy of the publishers) in articles from the pen of Professor Chassar Moir. The quality of their reproduction in this volume is a credit alike to him, to the publishers, and to their block-maker.

In the general letterpress, one finds major innovations in every section, although much of the original text is preserved. The authors have paid due regard to the classical tradition of obstetrics, and it is gratifying to notice the inclusion of many treatments of proved worth which modern teaching is inclined to treat in somewhat stepmotherly fashion. The reviewer, remembering his personal experiences in obstetrical practice in an area of endemic rickets, is gratified to observe that the chapter on destructive operations on the foetus is unabridged. It would be hard to find a more lucid description of a surgical procedure in any textbook and, so long as the need for such operations remains, specialists-in-training will be grateful for the written record of the experience gained by Professor Munro Kerr in that astounding Glasgow school of the early twentieth century. No modern accoucheur can count on securing such training. It is true that many will be without wish to do so, but Munro Kerr argues, with characteristic eloquence, the case for an enlightened use of craniotomy. Those portions of the work which bear the characteristic stamp of Professor Chassar Moir include a brief summary of his work on radiological pelvimetry. There is no doubt too that the section on deep transverse arrest of the head incorporates much of his practical experience, and is so great an improvement upon the treatment of this subject in the previous edition that one would like to have seen it expanded. Under the heading of injuries to the bladder, space is found for a summary of some of Professor Moir's important work on vesico-vaginal fistula. Elsewhere it is, very rightly, difficult to separate the work of the collaborators. They have blended their skills admirably, and it would be hard to pick out any portion of the work for special praise.

Similarly, it would be churlish to apply disparaging criticism on any large scale, although the book is not without faults, which will no doubt be remedied in due course. It is certain that many of these are attributable to the very long interval, no doubt unavoidable, which is understood to have elapsed between the preparation of the manuscript and the appearance of the book. It is disappointing in the section on radiological diagnosis of foetal deformities to observe no reference to the work of Hartley & Burnett (1943) on craniolacunia. The important paper of Knott & Blaikley (1944) on staphylococcal infections surely merits mention in the section on the prevention of infection, while the paper by Colebrook (1946) on the control of infection should have been considered. Indeed, this particular section requires rewriting to bring it

Continued at foot of page 93

[1] For particulars, see p. 122.

THE TEACHING OF BIOCHEMISTRY

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The importance, actual and potential, of biochemistry in relation to medicine is now generally accepted. Dr C. W. Carter and Professor R. H. S. Thompson state in the preface to their recent book, *Biochemistry in relation to medicine*[1]:

> The progress which is being made in the medical sciences by virtue of a biochemical approach renders it imperative for the medical graduate to be informed about the dynamic aspects of modern biochemistry.

" Dynamic" in this context is a word much in vogue. It is true that thermodynamics and reaction kinetics have their place in biochemistry, that there is a brisk turnover in enzymically catalyzed processes and that metabolic cycles elucidate much that was formerly obscure. It is also true that the actual molecules making up body tissues have been shown by isotope studies to be broken down and replaced at a more rapid rate than was to be expected. All this makes up an important part of the pattern of contemporary biochemistry but it is far from being the whole thing. Hopkins used the word dynamic to reinforce his teaching that the " traffic " in chemical substances was rapid and complicated in living things. Baldwin's well-known book, *Dynamic aspects of biochemistry* (Cambridge University Press, London, 1947) tells the story of a generation of progress along these lines and Schoenheimer's book, *The dynamic state of body constituents* (Oxford University Press, London, 1946) gives the whole subject a new twist. There is now a danger of either unduly restricting the scope of the word " biochemistry " or of so overloading the expression " dynamic aspects " as to deprive it of precise meaning.

The medical student needs in his preclinical years to acquire (i) an understanding of the fundamentals of chemistry and some facility in using its language, (ii) a substantial amount of rather miscellaneous information common to chemistry and biochemistry but chosen for its relevance, (iii) a conception of biochemistry as a " whole." He must inevitably learn his biochemistry in bits and pieces but the fact that they dovetail together must be kept before his mind. He is also learning anatomy and physiology and there is plenty to keep him busy! It is widely agreed that his teachers should make an effort to bring out the complementary characteristics of the physiological and biochemical approaches, and that the time devoted to normal physiology and normal metabolism is good preparation for studying the biochemistry of disease.

The complexity of this teaching problem is not generally appreciated. In most medical schools about 30 lectures are allotted to biochemistry proper, with perhaps 10 to the territory common to organic chemistry and biochemistry. Much of the practical work deals with necessary exercises inherited from the past and, when this indispensable minimum is done and the student has been introduced to modern techniques, there is relatively little time left for laboratory work planned specifically to illustrate modern concepts. A great deal therefore depends on the quality of the textbook which the student reads and re-reads, and it is very important that clinical teachers should know pretty clearly what the student has tried to assimilate and how far he has been successful.

The position today is roughly as follows: the biochemistry course proper begins with enzymes, their nature, properties and classification. This leads to the study of prosthetic groups, co-enzymes and digestion. Some physical chemistry is introduced and there is parallel practical work. The large topic of biological oxidations requires some knowledge about vitamins in order to appreciate co-enzyme action, and about haemoglobin, myoglobin and the cytochrome system. Electrolyte and acid-base equilibria need clear thinking in terms of elementary physical chemistry, and skilful piloting is necessary through what is often a maze of interpretation of vitamin and hormone function.

[1] For particulars, see p. 122.

OPERATIVE OBSTETRICS

Continued from page 92

in line with the changing outlook on the problems of infection resulting from the use of antibiotics. On page 53 the authors record that, whilst they regard themselves as free to teach to postgraduates that traction on the cord may be employed judiciously in the third stage (they admit their heresy), they do not regard themselves as free to do so when teaching undergraduates. There has been in the past a tendency to underrate the critical faculty and intelligence of the undergraduate, and one wonders if the authors would not do better to take the medical students more into their confidence. The section on faults in the expulsive forces might well be expanded somewhat in view of the fact that dystocia from this cause is found, relatively speaking, more frequently as the incidence of gross disproportion diminishes. It might be more logical to discuss constriction ring dystocia under this heading, rather than under abnormalities of the utero-vaginal canal, while a reference to the interesting paper of Louw (1948) would be valuable.

The book is printed on excellent paper. It is undoubtedly a distinguished example of the art of the medical publisher. The work of the book-binder is less satisfactory, and despite the most careful handling there is a tendency for the covers to come adrift.

There is no doubt that the current edition of this textbook is indispensable for the library of all who pretend to the thoughtful practice of obstetrics.

REFERENCES

Colebrook, L. (1946) *J. Obstet. Gynaec.* **53**, 114
Hartley, J. B. & Burnett, C. W. F. (1943) *J. Obstet. Gynaec.* **50**, 1
Knott, F. A. & Blaikley, J. B. (1944) *J. Obstet. Gynaec.* **51**, 386
Louw, J. J. (1948) *S. Afr. med. J.* **22**, 11

TEACHING OF BIOCHEMISTRY *R. A. Morton*

Most students find the study of vitamins and hormones attractive and easy at the stage of memorizing tidy little parcels of information. They take kindly to the descriptive aspects of absorption and intermediary metabolism, and a fair proportion like and are good at remembering rather complicated structural formulae. The real difficulty is that the cross-linking of topics is the heart of the matter. There is much to be said for a quick run over the ground followed by recapitulation and elaboration. Towards the end of the course the shadow of impending examinations makes factual information seem more important than comprehension.

All the foregoing is familiar to experienced teachers of biochemistry but it is entirely relevant to forming an opinion about a new textbook.

Dr Carter and Professor Thompson make a point of bridging the gap between practical work in the laboratory and theoretical instruction. Their book includes many practical exercises carried out in the medical and Honours physiology course at Oxford. A substantial part of the treatise is neither better nor worse than the corresponding chapters of other textbooks; it is straightforward, orthodox and clear. There is a rather definite bias towards experimental and clinical biochemistry; thus the Warburg apparatus is well described and much space is given to gastric and liver function and the testing of urine. On the other hand there is no systematic discussion of thyroxine, sex hormones or pituitary hormones; fat metabolism is treated briefly very early in the book and protein metabolism only incidentally. In addition to such curious omissions the level of discussion varies a good deal: thus the section on coagulation of blood is very interesting to anyone who already knows the elementary story, but difficult for the beginner; the same applies to the section on vitamin C. On the other hand energy metabolism is dealt with clearly but at a very elementary level.

The index contains a reference to pentdyopent but not to oestrogens, progesterone or corticosterone. How many readers other than chemists will know what an allophanate is? This uneven treatment will no doubt be rectified when a new edition is called for. This first edition is excellent for the clinical and postgraduate student wishing to refresh his knowledge and bring it up to date, and all teachers will find here something to admire and try out as well as something with which to disagree. Clinicians will obtain from it (in spite of its omissions) a good idea of the level of present-day elementary biochemical teaching but they should not imagine that the excellent bibliography of important papers will be much used by preclinical students.

Although it may be doubted whether the knotty problems of selection, order of presentation and integration in the teaching of biochemistry are brought appreciably nearer solution by this book, the work has genuine merits. It is an admirable supplement to a good course of instruction and some topics are dealt with unusually well.

A minority of able and enthusiastic students manage by the end of the preclinical period to get a unified picture of complex interrelations—the essence of biochemistry—but many fail in the time available to sort out the jumble of information they have acquired. Contributory causes are: first, that they have underrated the importance of knowing their *chemistry* properly and are seriously handicapped thereby, and second, that they do not appreciate the cumulative importance of recapitulation in their private reading in helping themselves to build up a unified picture.

Too much must not be expected of textbook or student and for many the stimulus of clinical study will bring biochemistry into focus. Dr Carter and Professor Thompson show awareness of this problem, and what may seem to one reader to be defects in their book may be merits to another.

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Annotations & News

FUTURE MEDICAL CONGRESSES

Cardiology. The Third National Congress of Cardiology will be held in the first fortnight of December 1950 at Valencia. Particulars may be obtained from the organizing secretary, Dr Don José Almela Guillén, 30 calle de la Paz, Valencia.

Gynaecology. The International Congress of Gynaecology will be held in Paris from 23 to 29 June 1951 under the patronage of the President of the French Republic. French will be the official tongue of the Congress. The general organizer is M. Maurice Fabre, 1 rue Jules-Lefebvre, Paris 9e, and enquiries by those wishing to submit papers should be addressed to M. Claude Béclère, 23 rue d'Artois, Paris 8e.

Industrial Medicine. The Tenth International Congress of Industrial Medicine will be held at Lisbon, from 9 to 15 September 1951. The general secretary is Dr Alex Ribeiro da Cunha, from whom information may be had at Service de Relations Internationales, Institut National du Travail et de la Prévoyance, Praça do Comércio, Lisbon.

Tuberculosis. The Tenth International Congress of Tuberculosis will be held in May 1951 at the Istituto Principi di Piemonte. The secretary general of the conference is Professor Gino Babolini, 76 Via S. Teresa al Museo, Naples.

ROYAL SOCIETY FELLOWSHIPS

The Royal Society, in March 1950, elected into the Fellowship of the Society twenty-five distinguished scientists. Among the new Fellows, we note with pleasure, the following who are working in medical research and allied subjects :

BORIS PETROVITCH BABKIN. Physiologist, McGill University, Montreal, Canada. Distinguished for his work on secretion by the digestive tract and on conditioned reflexes.

WILLIAM JOSEPH ELFORD. Biophysicist, National Institute for Medical Research, London. Distinguished especially for his researches on viruses, particularly on methods of determining virus size.

CECIL ARTHUR HOARE. Protozoologist to the Wellcome Laboratories of Tropical Medicine, London. Distinguished for his work on parasitic protozoa, especially the trypanosomes.

ARCHER JOHN PORTER MARTIN. Biochemist, National Institute for Medical Research, London. Distinguished for his work on the development of liquid-liquid partition chromatographic methods of chemical analysis.

RICHARD ALAN MORTON. Professor of Biochemistry, University of Liverpool. Distinguished for his studies on the chemistry and biochemistry of the fat-soluble vitamins.

RICHARD JULIUS PUMPHREY. Professor of Zoology, University of Liverpool. Distinguished for his researches on the sense organs and central nervous system of animals, particularly for his work on hearing in insects and man.

HENRY EDWARD SHORTT, C.I.E. Head of the Department of Parasitology, London School of Hygiene and Tropical Medicine. Distinguished for his work on protozoal diseases.

MAURICE STACEY. Professor of Chemistry, University of Birmingham. Distinguished for his researches in organic chemistry, especially his studies of the carbohydrates of animal tissue and of micro-organisms.

RICHARD LAWRENCE MILLINGTON SYNGE. Biochemist, Rowett Research Institute, Aberdeenshire. Distinguished for his application of the principle of partition chromatography to the separation of amino-acids and peptides.

TUBERCULOSIS IN MINING AREAS THE RHONDDA FACH SCHEME

Since the article in this number on pneumoconiosis in coalminers by Dr C. M. Fletcher and Professor J. Gough was written, the beginning of a new mass radiography scheme, the Rhondda Fach scheme, has been announced. The Rhondda Fach scheme is the name given to a project sponsored by the Pneumoconiosis Research Unit (P.R.U.) of the Medical Research Council, and is taking place in the Rhondda Fach—the Little Rhondda Valley in South Wales—which has a population of approximately 30,000. The primary aim of the scheme is to test a theory that the more serious forms (particularly progressive massive fibrosis) of pneumoconiosis among coalminers are due to a combination of the effects of that disease and of tuberculosis. Each member of this community will have an *x* ray of the chest, those of the miners and former miners on full-size plates taken by the mobile radiography unit of the P.R.U., and those of the non-mining population by mass miniature radiography methods. This decision results from experience that the 35 mm. films do not reveal early pneumoconiosis.

It is hoped that the scheme, which is likely to last more than five years, will help to solve two major problems : can the spread of tuberculosis be prevented with the help of mass miniature radiography ? and if so, will pneumoconiosis then cease to be a serious disabling disease ?

INDUSTRIAL AND SOCIAL OPHTHALMOLOGY EXHIBITION IN LONDON

The Exhibition of Industrial and Social Ophthalmology held at the London School of Hygiene and Tropical Medicine from 17 to 22 July 1950 was timed to coincide with the first post-war International Congress of Ophthalmology which was in session during the same period. It was the first demonstration of its kind ever offered to Congress delegates, and it focused both professional and lay attention on the important subject of industrial ophthalmology, a relatively new branch of industrial science.

The Exhibition presented numerous ways and methods of preventing eye accidents in industry, as well as the manner in which employers and employees can co-operate in the general promotion of visual health and safety. It also showed how much can be done to enable those whose vision has been seriously impaired, or lost, to lead a useful, interesting and independent life. The exhibits were divided into fifteen sections ranging from the use of optical devices in close work, eye safety devices, first aid and subsequent treatment of industrial eye injuries, to the early history of industrial ophthalmology, the manufacture and fitting of contact lenses, and the care of the blind.

MEDICAL PHOTOGRAPHY

An International Exhibition of Medical Photography was held from 12 to 24 June at 11 Chandos Street, London, W.1, the home of the Medical Society of London. The exhibition was sponsored by the Medical Group of the Royal Photographic Society of Great Britain.

Exhibits were in two main sections, prints and transparencies, and there was an excellent catalogue to guide visitors. As one would expect, most of the exhibits illustrated striking features of interesting and somewhat uncommon diseases. In addition to

British entries there were many from Switzerland, the USA, Australia, South Africa, Austria, Portugal, Sweden, the Channel Islands and the Gold Coast. It was a well-planned display and should encourage hospital authorities to make full use of their photographic departments.

APPROVED NAMES FOR PEST CONTROL PRODUCTS

The British Standards Institution has set up a committee with the following terms of reference: "To prepare standards for the nomenclature for insecticidal and fungicidal chemicals and other pest control products." The nomenclature will not conflict with the proprietary names, but will provide simple names by which the active ingredients of pest control products may be known. The committee is collaborating with Standards organizations in countries of the British Commonwealth, and with the USA Inter-Departmental Committee on Pest Control. The secretary of the British committee is Dr C. Tinker, British Standards Institution, 28 Victoria Street, London, S.W.1, from whom further information may be obtained.

INFERTILITY AWARD FOR OUTSTANDING RESEARCH

The American Society for the Study of Sterility offers an annual award of $1,000, known as the Ortho Award, for an outstanding contribution to the subject of infertility and sterility. The competition is open to those in clinical practice as well as to individuals whose work is restricted to research in the basic sciences. Essays submitted for the 1951 contest must be received not later than 1 March 1951. The Prize Essay will appear on the programme of the 1951 meeting of the Society. For full particulars, write to: The American Society for the Study of Sterility, 20 Magnolia Terrace, Springfield, Massachusetts, USA.

LEPROSY RESEARCH

We note with pleasure that the British scientist, Dr John Lowe, of the School of Tropical Medicine, Calcutta, has been awarded the "Prêmio Leprologia" (Prize for Research in Leprosy) for 1950, by the Academia Nacional de Medicina at Rio de Janeiro. Dr Lowe has been a British Empire Leprosy Relief Association research worker and has had wide experience in fighting leprosy in many countries, including India and Nigeria; he is also the author of many publications on the subject.

PUBLICATIONS AND REPORTS

Accidents: how they happen and how to prevent them, a new series of pamphlets to be published quarterly by His Majesty's Stationery Office, is issued by the Factory Department of the Ministry of Labour and National Service. The first number of vol. 1 (October 1949) describes thirty industrial accidents and suggests how each of them might have been prevented. They are arranged in sections according to the industry involved and some are illustrated with simple pictures.

Many industrial accidents occur because operators seem unaware that their machines can be dangerous. This is particularly true where process or woodworking machinery is used. Chemical accidents are difficult to guard against because the risk of being gassed when entering a harmless-looking plant or of being burnt by a corrosive liquid would not be obvious to most workers. Safety precautions against these accidents and those in building and structural work need keen supervision, as usually more than one person is injured.

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The *Bibliography of scientific publications of South Asia* is to be published by UNESCO at the Science Co-operation Office for South Asia, University Buildings, Delhi, India, at half-yearly intervals. It is intended to facilitate the exchange of information between the scientists of the region. The first number (January–June 1949) covered papers published during that period in India, Burma and Ceylon; a separate series will be issued for other South Asian countries. All branches of science are included in the bibliography, 25 of its 107 pages being devoted to "Medical sciences."

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El Consejo General de los Colegios Oficiales de Auxiliares Sanitarios de España has produced an account of the conference held in Madrid in April 1950, "El cáncer puede ser curado. Estado actual de la lucha contra el cáncer", under the chairmanship of Dr José Vidaurretta Aparicio. This is published in the April number of *Medicina y Cirugia Auxiliar* (Madrid).

NEW JOURNALS

The International Dental Federation announces the forthcoming publication of the *International Dental Journal*, a new quarterly review. The aim of the editors is to provide an accurate scientific review of progress in all fields of dental science and practice. The journal will be printed in English but a summary of each article, captions to illustrations, and a detailed list of contents will appear in French, German, Italian and Spanish. The first issue will appear in September 1950, and can be obtained from the distributors: Cassell & Co. Ltd., 37/38 St. Andrew's Hill, London, E.C.4.

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Argentina

We have received vol. 1, no. 2 (March 1950) of *Neuropsiquiatria*, published every three months at Buenos Aires, under the auspices of the Ministry of Public Health of the Argentine. Among the seven original contributions to this number are papers on Hallervorden-Spatz disease associated with gastromalacia, optic atrophy and neurosyphilis, and the action of glutamic acid in the central nervous system. There is also a large section of book reviews.

We have received the first number of *Prensa Pediátrica* (Buenos Aires). It is intended that this journal shall publish original articles, case reports, book reviews and abstracts, together with news items and notices of conferences. The present number (year 1, no. 1, September–October 1949) includes articles on streptomycin in the treatment of tuberculous meningitis (P. de Elizalde), protection of the infant against congenital syphilis (M. L. Saldún de Rodríguez & J. M. Portillo), and a study on the nutrition of children in the institution "Crescencia Boado de Garrigos" (A. Giussani).

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Mexico

We have received the first number of *Boletin Tisiológico Dispensarial* (Mexico, D. F.), a publication appearing every two months and produced by the Comité Nacional de Lucha contra la Tuberculosis of Mexico. There are clinical notes on a case of coccidioidomycosis, three original articles, and a section of abstracts from world literature on tuberculosis.

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Spain

Acta Ginecologica (Madrid) of which we have received vol. 1, no. 2 (1950) is edited by Dr J. Boletta Llusiá with the collaboration of doctors from all parts of Spain, Spanish America and Mexico. The number includes original articles on vaginal hysterectomy in cases of prolapse (C. Zuckermann), rupture of the uterus (C. Pino Alvarez), a case of true hermaphroditism (M. Rabadán, F. Nogales, A. de la Peña & J. Botella) and the relation of alkaline phosphatase in blood and urine during pregnancy (V. Conill Serra). There are also sections of abstracts from world literature, notes on conferences, and book reviews.

JOURNALS NEWLY RECEIVED

The February number of the *Journal of Bone and Joint Surgery* (London & Boston) is the first number of vol. 32B. This journal is the official publication of orthopaedic surgeons both in the British Commonwealth and in the USA. The list of contents for February shows that contributions come from many parts of the English-speaking world; the editor is, however, most anxious to publish suitable articles from any country, and facilities for translation are available. Numbers are published alternately in Great Britain and the USA, and it would be difficult to find a better-produced journal of its type than this. The most interesting new work in this number is a review of some cases of neonatal sciatic palsy by W. H. Fahrni of Vancouver and the comment on this review by B. L. McFarland of Liverpool. Fahrni suggests that the palsy may be caused by the pressure of a foetal hand on the sciatic nerve trunk: McFarland's opinion is that the cause is the injection of noxious drugs into the umbilical artery. There are many other contributions, and also book and historical reviews.

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The *Health Bulletin* (Edinburgh) has just published no. 2 of vol. 8. This journal is easy to read and contains useful articles on burns and scalds and on changes in mortality rates in Scotland in recent years. Among other articles are "A poliomyelitis survey" and "The problem of the elderly", a report of an address by Sir Andrew Davidson. The *Bulletin* is issued by the Chief Medical Officer of the Department of Health for Scotland.

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The *Bulletin de la Société Française de Phlébologie* (Paris) is in its third year of publication. The number for January-March 1950 comprises about 40 pages. It contains reports of two meetings held in October and December 1949, the first dealing chiefly with the treatment of venous thrombosis and the second with new sclerosing agents. There is also a list of current French publications on phlebology. The journal appears four times a year.

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The *Tohoku Journal of Experimental Medicine* is an official organ of the Tohoku University, Japan, for the publication of research in experimental medicine. Three to four volumes are issued each year and the articles are written in English, French, or German. We have received vol. 51, no. 1–2, 1949.

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We have received nos. 1 and 2 of vol. 35 of *Anales de la Facultad de Medicina de Montevideo*. This journal appears monthly and consists almost entirely of original papers presented by the Medical Faculty of Montevideo. In no. 1, for example, there are articles on the confirmation of torulopsis neoformans in histological sections, and on the relation of the thymus to the reticuloendothelial system; in no. 2, there are contributions on pain in surgery, varicose veins, phlebitis and venous thrombosis, and on causalgia.

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The following journals have also been received:

Boletin de la Maternidad Concepción Palacios (Caracas), vol. 1, nos. 1 & 2, 1949

Boletin de los Servicios Médicos, Universidad de San Marcus (Lima), vol. 3, nos. 3 & 4–5, 1948 & 1949

Enfermeria. Archivos del Ministerio de Salud Pública de la Nación (Buenos Aires), vol. 1, no. 2, 1950

Folia Clinica et Biologica (São Paulo), vol. 16, 1949

Journal of the California State Dental Association (San Francisco), vol. 26, no. 3, 1950 (Supplementary issue—'Sugar and Dental Caries. A Symposium")

Les Monographies Médicales et Scientifiques (Paris), no. 6, 1950

Omnia Medica (Pisa), vol. 27, nos. 7–12, 1949

Omnia Therapeutica (Pisa), vol. 1, no. 2, 1950

Ortodoncia. Organo de la Sociedad Argentina de Ortodoncia (Buenos Aires), year 13, no. 26, 1949

Puericultura. Revista Mexicana para el Estudio de los Problemas de Protección Integral a la Infancia (Mexico, D. F.), vol. 1, no. 1, 1950

Revista Médica Pasteur. Organo Oficial de la Asociación Médica Franco Mexicana (Mexico, D.F.), vol. 1, no. 1, 1950

Sind Medical Journal (Karachi), vol. 22, no. 3, 1949

Türkiye Genel Kimyagerler Kurumu Dergisi (Ankara), vol. 2, nos. 6, 7 & 9, 1949 & 1950

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Historical Notes

SOME EARLY BRITISH WORKS ON OCCUPATION IN RELATION TO HEALTH

There was no great interest in Britain in the association between occupation and health until the 19th century. At that time the deepening of interest was connected with the sanitary reform movement, and was a branch of this movement in which Britain took a leading part.

Nevertheless, it is perhaps not without significance that, within five years of its first publication in 1700, Bernardino Ramazzini's classic book, *De morbo artificum diatriba*, Capponi, Mutinae, was translated into English and published in London (1705). The translation remains anonymous and in 1746 Dr Robert James re-issued it as his own, with the addition of a translation (which James made himself) of the Supplement added by Ramazzini to the original work in 1713. James's book was reprinted under a different title in 1750. Diseases of miners, where the association is more obvious, are in a rather special class, and books on these diseases had appeared before Ramazzini's.

As with so many important medical developments, interest in occupational health owed much to the stimulus of the Edinburgh School. In 1809 Dr John Roberton of Edinburgh published, in two volumes, *A treatise on medical police*, which was the first notable treatise in English upon the subject of public health. He listed " occupations, modes of living and manners in general " as among the " artificial causes " of disease.

> There are innumerable occupations, the prosecution of which must be less or more productive of disease: and the general importance of this enquiry must be at once appreciated,

wrote Roberton, under the heading, " Of occupations." Because Roberton held the contemporary opinion of the transmission of disease by the " atmosphere "—a hypothesis which enabled the early sanitarians to effect great improvements—he dwelt upon this, and described, for instance, night employments as being highly dangerous " particularly when the air is foggy." He referred to specific industrial poisons, such as white lead :

> Partial paralytic disorders are even very common among those printers who are much in the habit of handling types, particularly compositors. These diseases often affect them only in a slight degree, and by refraining from work for a few days or weeks, they entirely disappear. At other times, one or both hands are rendered completely powerless: and, independently of the very greatest attention that can be paid to them, remain often in that state for many months.

Roberton, like Ramazzini, included the categories of non-industrial occupations, and described the " two principal causes of disease among those following the learned professions " as " the perpetual labours of the mind, and the constant inaction of the body." He advocated " police for occupations " to prevent industries harmful to health being carried on in cities ; this suggestion again was a product of the atmospheric theory.

It was a doctor in one of the industrial cities formed as a result of the industrial revolution in Great Britain who carried out at Leeds the first large-scale scientific investigation into the relation of health and disease and environment. He was Dr Charles Turner Thackrah (1795–1833), who, appropriately, was connected with the founding of one of the newer medical schools, that of Leeds. The index to the first edition of his book (1831) lists 149 employments, covering such a wide range as accountants, worsted spinners, horse-dealers, lawyers, postilions, slubbers, waiters at inns, and staymakers. Thackrah thus explained his method of investigation :

> Myself and my pupils have personally and carefully inspected the state of the artizans in most kinds of manufacture, examined the agencies believed to be injurious, conversed on the subject with masters, overlookers, and the more inteligent workmen, and obtained many tables illustrating the character of the disorders prevalent in the several kinds of employ.

Thackrah's book was a model for all subsequent inquiries of this kind. Its popularity, which is indicative of the interest that was being taken in this new branch of medicine by the profession, is shown by the rapid sale of the report and the fact that a second edition, enlarged to give details of 120 other occupations, was published a year later (1832). In his preface to this edition, Thackrah wrote :

> Still much, very much remains to be done: and I would earnestly solicit the profession to aid, extend, and correct these important investigations.

Thackrah himself was able to do no more. A year later he died, at the age of 38.

Thackrah divided those employed into the following classes: operatives, dealers, master-manufacturers and merchants, and professional men ; in the second edition he included notice of a further class—" men independent of business and labour." Not the least interesting part of his reports are the glimpses which they give of ways of life in his day. Thus we read that butchers ride on horse-back to markets : " They are well known to ride fast, and to take often long journeys." It is noted that the posture of clock-makers is varied and moreover they often travel to repair clocks in the country, and they are generally healthy. Watchmakers, on the other hand, have a much worse employment. Brickmakers, although they work half-naked and with their bare feet in a puddle all day, are not more liable to catarrh, pneumonia and rheumatism than men whose work is under cover and dry. Thackrah also discussed specific industrial hazards, such as dust and " odours and gaseous exhalations," and methods of prevention, and stated : " The employment of young children in *any* labour is wrong." He was of the opinion that employers have a right to concern themselves with how their artisans spend their evenings. He stressed the importance of fresh air and exercise, and called for a reduction of hours and the paying of more attention to the health of both workmen and masters.

The influence of Thackrah's book was not confined to Britain. A prize for an essay on a chosen subject was offered annually by the Medical Society of the State of New York ; the subject in 1835 was occupational health and the prize was won by Dr Benjamin W. McCready. The title of McCready's book, published in 1837 and reprinted in 1943, follows that of Thackrah's, and it was the first investigation of its kind in the United States of America.

In the same year, 1832, in which Thackrah's book was published there appeared the second edition of a pamphlet by Dr J. P. Kay. This dealt with political and sanitary reform, attacking the Poor Laws as well as sanitary conditions, and it gave an account of a cotton operative's day, referring to the effect of " the dull routine of a ceaseless drudgery ".

Towards the end of the century, in 1876, Sir Benjamin Ward Richardson[1] published a semi-popular work entitled *Diseases of modern life*. This is not of the same type or importance as Thackrah's, but it is interesting to note that in it emphasis is being given to psychological effects. Journalists (" copyists who vend the news ") have " no further waste of nervous force than is expended in attention," although long hours " coupled now and then with a little too much negligence in eating, drinking, and avoiding, make them dyspeptic and nervous." " The higher class of men of letters,—they who think as well as write, are subjected to greater perils," again of a nervous kind. Richardson remarked of the commercial classes that they

> rarely possess that dispassionate and thoughtful temper which comes, so naturally, to the minister, the lawyer, and the physician, and the reason of this is simple enough. They are absorbed, without diversion of mental exercise, in their own affairs.

This is similar to Thackrah, who had written of shopkeepers that they presented " a sad picture of an unnatural life, which sinks alike mental and corporeal energies."

By 1876 that most important characteristic of modern city life—the lengthening journey to and from work—was becoming established. I believe that Richardson was one of the first medical writers to consider its implications.

> The haste made to catch the train: the confusion, noise, and bustle of the railway station ; the shriek of the engine ; the start from and stoppage at various stations ; the perpetual vibration communicated through the carriage to the body ; the closeness of the carriage or the draught through it ; the desire in the carriage to fill the time by reading, controversy, joking or games of chance ;—these influences all contribute most materially to injure the life of the man who subjects himself to them, be he ever so strong, careful and collected.

Richardson described what one may term " railway syndrome." Those who feel, on seating themselves in the carriage, " a peculiar restlessness and even faintness, which passes away so soon as the carriage is in motion, but which returns with so much increased intensity as the train stops " have an indication " of threatened organic change in the nervous matter." Less dangerous is a peculiar sensitiveness in the spine, followed in the course of time by a feeling of " want of steadiness in the lower limbs on first alighting from the train."

[1] See Book Reviews, p. 121.

It is noteworthy that the effect of study upon health, a subject on which papers have been published of recent years in medical journals, engaged the attention of all these early writers. Thus Roberton, who had experience of Edinburgh medical students, referred to the " destructive habit of studying all or the greater part of the night ". Thackrah stated that the mortality among medical students was great, and wrote :

> Pupils sent to distant medical schools at the end of their apprenticeship, and thus placed suddenly in a scene of dissipation, without governor or adviser,—mixing too with large masses of youths similarly situated,—suffer from the evils and disease, which irregularity produces. While the steady youths, attending the hospitals, dissecting, hearing various lectures, and preparing for examinations . . . are severely injured by the great application of mind.

Thackrah had studied at Guy's Hospital. He suggested that " scientific education " for medical students might be conducted in large measure in the country, and the youths might obtain knowledge " more fully, more slowly, and therefore more securely."

Both Thackrah and Richardson discussed whether medicine was a healthy occupation : Thackrah, the doctor in an industrial area, wrote :

> As a profession, we are by no means healthy. Indigestion is general, and diseases of the lungs and blood-vessels are frequent . . .

Richardson, the London consultant, held a very different opinion :

> *Medical* men, as a class, are remarkably free from disease when all the details of their lives are taken into consideration . . . I have not a doubt, and I speak from a large experience of them and their ways, that, taking them all in all, the members of the Esculapian fraternity are the cheerfullest and the happiest of any section of the community.

Laurence Dopson

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JOHANNES EVANGELISTA PURKINJE
1787–1869

Johannes Evangelista Purkinje—or Jan Evangelista Purkyně, to give his name in its vernacular form—ranks with Jan Hus and Amos Comenius among the great glories of the Czech nation. In the course of his long life he made contributions of fundamental importance to almost every branch of physiology. In medical terminology his name is commemorated by at least eight eponyms, the best known of which are the " Purkinje cells " of the cerebellum (1837) and the " Purkinje fibres " of the heart (1839). Unlike many men of genius Purkinje received ample recognition in his lifetime. When he returned to Prague in 1850, after 26 years spent in a foreign country, he was provided with a splendid laboratory, and in his old age he was surrounded by the unbounded affection of the whole nation. He became a leader of the Czech nationalist movement and a member of the Bohemian Diet. Recognition of Purkinje was not confined to his native land. In 1850 he was elected a Foreign Fellow of the Royal Society, and he was a corresponding member of the French Institute and of the academies of Vienna, Berlin and St Petersburg.

Although there is no definitive biography of Purkinje a great deal has been written about various aspects of his life and work. It is a measure of the impact which he made upon so many fields of knowledge that he has received attention from writers of all kinds—

JOHANNES EVANGELISTA PURKINJE
1787–1869

Wellcome Historical Medical Museum

physiologists, pharmacologists, embryologists, ophthalmologists, psychologists, microscopists, anthropologists, botanists, and educationalists. The works of Purkinje are very little known in the original ; the results of many of his most important researches were published in obscure dissertations by his pupils and many of his own papers appeared in journals which are now rare and unprocurable except in the largest libraries.

Czech physicians have never neglected their great countryman, and in recent years they have published a mass of Purkinje literature comprising annotated editions of his writings, biographical sketches, and critical studies. The most important of these works is the *Opera omnia*[1] of Purkinje published by the Association of Czech Physicians and the Purkyně Society of Prague. The first volume of this edition of the Collected Works was published in 1918 ; the fourth volume appeared in 1948 but has only recently been received in this country. The fifth volume is to be published shortly. This work is a very fine production, being beautifully printed and adorned with reproductions of the original illustrations and with portraits of Purkinje at different ages. In 1948 the University of Prague—the oldest in Central Europe—celebrated the six hundredth anniversary of its foundation by the Bohemian King Charles IV. The Medical School of the University marked this great occasion by publishing a series entitled *Opera Facultatis Medicae Universitatis Carolinae Pragensis*. The first volume* of this series is devoted to the *Opera selecta*[2] of Purkinje, who was, as the editors of the volume recall with pride, once a student and later a professor at the ancient university. The *Opera selecta* is a beautifully printed volume containing, in addition to the selected texts, a reproduction in colour of P. Maixner's portrait of Purkinje, a biographical sketch which appears in Czech, Russian, English and French versions, and a list of writings about Purkinje. The book was edited by a committee consisting of Drs Z. Frankenberger, F. Karásek, V. Laufberger, K. Hübschmann, V. Kruta and F. K. Studnička. It contains four of Purkinje's longer works (those on the developing egg, finger prints, subjective vision, and the cellular

* For particulars, see p. 122.

theory), dissertations by his pupils that contain reports of his researches, and many of his shorter papers.

Another notable contribution to Purkinje literature is the selection from his correspondence[3], edited by Dr Jaroslav Jedlička in two volumes and published under the auspices of the Czech Medical Society in 1920–25. These volumes contain letters exchanged between Purkinje and scientists, literary men and statesmen in all parts of Europe; of special interest are the 22 letters written to Purkinje by the Baroness Adelaide Desfours. In 1937 the Purkyně Society of Prague, an association founded in 1935 for the study of the life and work of the great scientist, published a volume, *In memoriam Joh. Ev. Purkyně, 1787–1937*. This memorial volume contains 13 essays by Czech scientists on different aspects of Purkinje's work.

Johannes Evangelista Purkinje was born at Libochowitz in Bohemia on 17 December 1787. He attended school in his native village and was then sent as a chorister to the Piarists in Moravia, under whom he made great progress in the study of languages. For some time he taught in the Order and he later acted as a private tutor. In 1819 he graduated in medicine at Prague, his inaugural dissertation being an important work on the subjective phenomena of vision. This work won him the friendship and patronage of Goethe, through whose influence and that of Humboldt he was in 1823 appointed professor of physiology and pathology at the University of Breslau. He was at first coldly received, but gradually his personal character and exceptional attainments gained recognition. There was one particularly troublesome episode when he asked for a microscope, for none of his predecessors had had anything to do with such new-fangled notions. In 1824 he started a physiological laboratory in his own house, and here he carried on his researches until 1839 when the Prussian government erected a Physiological Institute for him at Breslau—the first of its kind. By this time he had many pupils. In his relations with other scientific workers he was particularly chivalrous and open-handed. It was Purkinje's habit to push on rapidly from one piece of research to another, leaving the details to others. His genius drove him to explore new frontiers. The writings of few scientists contain so much stimulating data and so many suggestions for further research. He enlarged the bounds of knowledge in so many directions that it is difficult to summarize even his major achievements.

As previously stated, his first work was in physiological optics. He was a pioneer in the description of most of the subjective visual figures, and his experiments upon the production of vertigo were the starting-point of modern work on nystagmus. His method of lighting the retina, his measurements of the curvatures of the lens and cornea, and his studies with mirrors of the refracting surfaces of the eye led directly to the invention of the ophthalmoscope.

In microscopy he made great technical advances, being the first to prepare sections with the microtome instead of free-hand with a razor and to make preparations on glass slides with Canada balsam. He was a pioneer in photomicrography. He made good use of his technical skill in exploring the structures of the skin, bones, blood-vessels, seminal vessels and teeth. In 1825 he described the germinal vesicle in the embryo, and in 1839 he introduced the term "protoplasm." He discovered the sudoriferous glands of the skin with their excretory ducts (1833), and in 1823, almost 70 years before Francis Galton, he described the unchanging character of fingerprints, giving accurate figurations of the same. In 1834–35 he wrote with Gabriel Valentin his famous essay on ciliary epithelial motion and by 1837 he had recognized the similar cellular structure of plants and animals. He was further distinguished as a pharmacologist, and carried out unpleasant and sometimes dangerous self-experiments on the action of camphor, opium, belladonna, stramonium, and turpentine. His "minor" researches extended into many fields: he noted that deaf-mutes can hear through the bones of the skull; studied the peculiar formation of the skin of cucumber plants; wrote a paper, "On the world of dreams", in which he anticipated some of Freud's theories: and carried out important work on artificial digestion.

In 1850 Purkinje returned to Prague as Professor of Physiology. The days of his greatest discoveries were over, but he continued to act as an intellectual ferment and his pen was never idle. He busied himself in Czech politics, founded and edited a journal of natural history and translated the lyrics of Schiller into Czech. As an octogenarian he continued to study languages—he learnt the difficult Magyar tongue—and to practise his violin. Purkinje's early experience as a teacher had given him an abiding interest in pedagogics. He was a firm supporter of the ideas of Pestalozzi and, being himself an ardent gymnast and advocate of physical culture, it is not surprising that he was one of the founders of the Sokol movement. His death, after a short illness, on 28 July 1869, was mourned by every class of society in Bohemia.

Purkinje was not only a great scientist; he came very near to the Greek ideal of the "whole man". The pious care of his countrymen has now provided these admirable editions of Purkinje's writings which cannot fail to make his achievements and his personality known to ever widening circles.

W. J. Bishop

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LORD LISTER: HIS LIFE AND DOCTRINE 1827–1912

The modern surgical operation is a spectacle which, by way of the film and the illustrated magazine, has captured the popular imagination. To the early H. G. Wells the aseptic scene with all its attendant ritual would have seemed a Martian fantasy, but to the surgeon of 1850 it would have been something quite inconceivable, for there was nothing in the surgery of that day to hint at any such development, and the principle of which it is the material expression was not given to the world until the year 1867. In Westminster Abbey there is a small tablet commemorating Lister, the man who made surgery such a life-saving procedure, but in every town and city throughout the world will be found his true memorial—the operating theatre in every local hospital.

The literature on Lister's life and work grows with every year. After Rickman Godlee's biography of his celebrated uncle (*Lord Lister*, Macmillan, London, 1914) had been published it might have seemed that little more remained to be said, but every generation prefers and demands books written in its own idiom. Douglas Guthrie's new study[1] of Lister is fitted for the hurried age in which we live. Short, informative and readable, it gives all the essentials of a long career pursued with an unswerving purpose and a single-minded devotion rare even among the greatest of a profession remarkable for those qualities.

By ordinary standards Lister's life was smooth and uneventful, and crowned at the end with a measure of worldly success and recognition such as is given to few pioneers. He was born at Upton, near London, on 5 April 1827. His family were members of the Society of Friends and his father, Joseph Jackson Lister, F.R.S., was well known as the microscopist who introduced the achromatic lens. An enthusiastic naturalist at an early age, young Lister was determined to become a surgeon. After graduating, first in arts and then in medicine, at University College, London, he embarked upon a series of physiological researches on the structure of the iris, the flow of chyle, the cutaneous pigmentary system of the frog, and the early stages of inflammation in tissue. This experience undoubtedly paved the way for his great work on the nature of sepsis and the means of preventing it.

Encouraged by William Sharpey, professor of physiology at University College, Lister decided to gain surgical experience under the famous James Syme and he left London for Edinburgh in 1853 intending to stay no more than a year. He remained there until 1860, first as Syme's dresser, then as house surgeon, and finally as assistant surgeon and lecturer in the medical school. In 1860 he was made professor of surgery in Glasgow University and in 1861 surgeon to the Glasgow Infirmary. There the wards were notorious incubators of hospital gangrene, pyaemia, erysipelas and tetanus, and Lister found ample material for his continued preoccupation with the problems of inflammation and postoperative sepsis.

Long before Thomas Anderson, professor of chemistry at Glasgow, drew his attention to Pasteur's early researches in 1865, Lister had already come to the conclusion that

> the essential cause of suppuration in wounds is decomposition, brought about by the influence of the atmosphere upon blood and serum retained within them, and, in the case of contused wounds, upon portions of tissue destroyed by the violence of the injury.

[1] For particulars, see p. 122.

He knew already that it was not the air itself but something in the air which was the causative agent and, leaping at the explanation implied in Pasteur's work, he was the first in the field in that ceaseless war against "germs" which is so characteristic of modern medicine. He called his discovery "the antiseptic principle" because he chose to use chemical means to destroy them. "Asepsis" does not differ in principle from "antisepsis" but only in the means employed, and those who think that Lister's achievement began with the carbolic spray and ended with its abolition overlook this vital fact.

Just when Lister was casting about for some suitable antiseptic the experimental use of carbolic acid on sewage at Carlisle met with striking success and he decided to try it in his surgical cases in the Glasgow Infirmary. Not content with treating the skin of the patient, the instruments and the surgeon's hands, he introduced the carbolic spray in order to destroy the germs in the surrounding air. As it later appeared, this was not so important a source of infection as he believed and the spray was abandoned. These measures met with such immediate and overwhelming success and produced such a sensational drop in the figures of postoperative mortality that one might justifiably imagine that they were immediately imitated throughout the world; but outside Lister's immediate circle they were accepted reluctantly, and much more readily in France and Germany than in Great Britain.

Ten years after the publication of his first classic paper, "On a new method of treating compound fractures, abscesses, etc.", in the *Lancet* (1867), having won over his colleagues, first at Glasgow, and then, from 1869, in his capacity of professor of clinical surgery, at Edinburgh, he returned to London to take the chair of surgery at King's College. After lecturing to enthusiastic audiences of hundreds in the Scottish capital he was greeted in London by a handful of indifferent and apathetic students and a body of sceptical colleagues. Like all such battles, the battle for antisepsis had to be fought many times before it was securely won. Only when his international fame could no longer be ignored did some of the "diehards" capitulate, although even after the turn of the century, when masks, caps and gowns, and even rubber gloves, were the standard in the best hospitals, there were still a few individuals who clung to the bloodstained frock-coat and who regarded even aesthetic cleanliness as an unnecessary fad.

Lister was the most patient and the most modest of men. Unruffled by opposition he continued his experiments with various techniques—the catgut ligature, drainage tubes, and absorbent gauze—designed to minimize the risk of infection. Many of these were carried out on animals, and he attempted to use his influence with Queen Victoria to dampen her ardour for the anti-vivisectionist cause.

Two years after his triumph at the International Congress of 1881 he was made a baronet, and in 1897 a peer, the first medical man to be so distinguished. For nearly fifty years he found in his wife Agnes, the daughter of James Syme, the perfect companion, and after her death in 1903 he retired more and more from public life. Touched by the messages which poured into his house at Park Crescent on the occasion of his eightieth birthday in 1907, he wrote to his brother, "What a change of opinion has taken place during the years in which I have been doing nothing!" He died at Walmer, in Kent, on 10 February 1912, at the age of eighty-five.

In his person and character, as his portraits well show, Lister was a man to inspire perfect trust and confidence in his patients and loyalty and devotion in his assistants. There are few more perfect models for the young and his is a story which should be known to every student. Dr Guthrie's book, beautifully illustrated and produced by Livingstone of Edinburgh, should become a treasured possession on their shelves.

F. N. L. Poynter

WILLIAM WITHERING OF BIRMINGHAM 1741–1799

Withering's fame today in medical circles rests upon a single book, his celebrated *Account of the foxglove, and some of its medical uses* (Robinson, Birmingham, 1785), the pharmacological classic on digitalis which has now become one of the most sought-after treasures of the medical bibliophile. Among botanists he is remembered as the author of the first British publication on botany that was arranged on the Linnaean system, and by the plant, *Witheringia solanacea*, named in his honour. He is not unknown to chemists and mineralogists, for he made serious contributions to both of their sciences, and even the archaeologist writing the history of the stone circles at Avebury and Stonehenge would have occasion to mention the interest which Withering showed in the preservation of those ancient monuments.

If these statements conjure up a picture of a leisured and wealthy eighteenth century dilettante it is salutary to consider the details of a career which had room for such variety. Born at Wellington in Shropshire in 1741, Withering was the son of an apothecary and came of a family which had been settled in the county for many generations. He studied medicine at Edinburgh and took the degree of M.D. in 1766, whereupon he accepted the post of physician to the newly established Staffordshire Infirmary and remained there for nine years. There he wrote his first great work, the *Botanical arrangement of all the vegetables naturally growing in Great Britain* (T. Cadel & P. Elmsley; G. Robinson, Birmingham, 1776), which ran into 14 editions and won him an international reputation as a botanist. It was still a standard work within living memory, for the last edition was published in 1877.

With the rise of Birmingham as a prosperous industrial city it became a magnet to men of ability and ambition in the surrounding counties, and in 1776 Withering was appointed physician to the General Hospital there. A busy practice which involved him in long and tedious journeys, often as much as 6,000 miles a year by horse-back, did not prevent him from following his bent in those branches of science which appealed to him and he found congenial company in the well-known "Lunar Club," a Birmingham scientific society which held its meetings whenever the moon was full. There he moved in a circle which included such well-known men as Erasmus Darwin (grandfather of Charles Darwin), James Watt, Matthew Boulton, Josiah Wedgewood and John Baskerville, and among the distinguished visitors whom they entertained from time to time were Sir William Herschel, Sir Joseph Banks, Benjamin Franklin and Pieter Camper.

It was doubtless Withering's preoccupation as a botanist which made him determine to investigate the grounds for a belief among the local country people that the leaves of the foxglove were efficacious as a remedy for dropsy. He set about this task in a truly modern way, making prolonged clinical trials, paying particular attention to dosage and to methods of preparation and administration, and taking careful note of its effects. His *Account of the foxglove* is remarkable for a scientific objectivity rare in the medical literature of the time. He reported failures as well as successes, and although he still regarded dropsy as a primary disease he found it possible to indicate that kind of dropsy (now known to be of cardiac origin) likely to benefit from the administration of digitalis.

Had Withering enjoyed good health it is probable that he would have made other equally important contributions to pharmacology, but for many years he fought against pulmonary tuberculosis and in his closing years made two voyages to Portugal in a vain search for health. He died at Birmingham on 6 October 1799 at the age of fifty-eight. On the black marble tablet which commemorates him in Edgbaston Old Church there are representations of *Digitalis purpurea* and of *Witheringia solanacea*.

It is extraordinary that a life which offers so much interest should have had to wait a hundred and fifty years for a full-length biography, but if this tribute has been too long delayed it is paid adequately in the book[1] which Professor K. Douglas Wilkinson of Birmingham now gives us. Enriched by numerous hitherto unpublished letters and by a wealth of illustration, it records not only the life of Withering but paints most vividly the circle in which he moved. In the last quarter of the eighteenth century were being laid the foundations of the great city of Birmingham as we know it today. In that home of many talents, thriving, industrious, and bursting with scientific curiosity and ingenuity, Withering found his spiritual home. It is fitting then that its name should appear in the title of this book by Professor Wilkinson and the late T. Whitmore Peck, for it is not only the most complete account we have of the man whom Osler regarded as one of the greatest of English physicians, but also a lively picture of Birmingham during one of the most formative periods of its history.

F. N. L. Poynter

[1] For particulars, see p. 122.

Book Reviews

MEDICINE

Practical Procedures in Clinical Medicine

R. I. S. Bayliss. London : J. & A. Churchill Ltd., 1950. viii + 445 pages ; 62 figures. 22 × 15 cm. £1 5s. [£1.25]

(i) Injections and the collection of blood ; (ii) disorders of the alimentary tract ; (iii) disorders of the cardio-vascular system ; (iv) disorders of the blood ; (v) parenteral infusions ; (vi) examination of urine and tests of renal function ; (vii) disorders of the liver ; (viii) disorders of the respiratory system ; (ix) disorders of the central nervous system ; (x) endocrine and metabolic disorders (xi) radiology in clinical medicine ; (xii) miscellanea. Index.

Undergraduate medical education rightly concerns itself with general principles, but the more complete this concentration on fundamentals may be, the more difficult does the young practitioner find the transition to responsibility for the detailed investigation of his patients. It is the need to provide the practitioner with these details that led the author to write this book. In its twelve chapters a wealth of useful information is available, much of which cannot be conveniently found elsewhere. The author considers in each chapter the investigation of diseases of one particular system, e.g. the cardiovascular, respiratory and nervous systems, and gives precise details of the techniques of those tests which the physician is accustomed to carry out for himself, and details of the materials required by the laboratory for more complicated tests or those entailing reference to the original literature. In every case a critical appreciation is given of the interpretation of the investigation. A chapter is devoted to radiology in clinical medicine, and the final chapter, headed " Miscellanea", is a mine of useful information, ranging from a table of atomic weights to a table giving the period of incubation and infectivity of the common infectious fevers.

It is understandable that in the first edition of a work of this kind there should be some errors of fact, just as it is clear that the author is less happy in some aspects of clinical investigation than he is in others. The number of errors is, however, commendably small and none are of fundamental importance. The reader may be surprised to notice that the use of the bacteriological examination of the stools is dismissed (on page 51) in three and a half lines, with no mention in the index of the use of the rectal swab or the throat swab, but it would be wrong to complain of omissions in a book of this type. The author has set out to give the physician a useful guide to the investigation of disease, and he has succeeded. May we hope that readers of this book, and there will be many, will help the author by pointing out omissions and improvements, so that in subsequent editions it will deservedly rank as the essential vade mecum of the practising physician? This book can be confidently recommended ; everyone practising medicine will derive some benefit from reading it.

H. B. May

Applied Medicine

G. E. Beaumont. London : J. & A. Churchill Ltd., 1950. ix + 540 pages ; 74 figures. 24 × 16 cm. £1 10s. [£1.5]

(i) Descriptive cases ; (ii) short notes on cases ; (iii) cases demonstrated at the bedside by question and answer ; (iv) idle thoughts. Index.

In this book is concentrated the wisdom of an extensive and penetrating clinical experience. Dr Beaumont is widely known as the author of many deservedly popular textbooks of medicine of the conventional type, but in *Applied medicine* both the approach and the content are unusual. He divides his text into four parts. Part I describes in detail over 30 cases from his records, designed to illustrate the principles of diagnosis, the help which ancillary investigations can give, and the need for considering the patient and not simply his " disease " in treatment. Each case is illuminated by a critical comment which exemplifies the methods of the practising doctor. Dr Beaumont is no narrow specialist : his examples range over the whole body ; nor do they neglect the mind. Errors of diagnosis are acknowledged and the vicissitudes of disease are stressed. There is a wealth of apt quotation and historical anecdote which reveal an enviable erudition.

In Part II are given short notes on 17 cases which illustrate how clinical acumen may throw light on the obscure diagnostic problem, and the rarer manifestations of disease, e.g. the baffling pyrexia whose cause is suggested by the love-birds in a cage in the conservatory ; acute alcoholic poisoning in a boy due to absorption of surgical spirit lavishly applied to the shaven legs ; the dislocated jaw simulating facial paralysis ; the association of bronchiectasis with infective arthritis.

Clinical ward teaching of the " question and answer " type is recorded in Part III. The commoner symptoms and signs, their mechanisms and their causes are here discussed in a manner which will certainly excite the interest of students and probably their envy, for few will have been fortunate enough to have been disciples of teachers whose knowledge, wisdom, experience, wit, forbearance, and clarity of exposition approach Dr Beaumont's. It is perhaps fair comment on this text that though some students are fortunate in their teachers, here is a teacher fortunate in his students. Not only do they ask Dr Beaumont just the questions which he would desire, but even their wrong answers are timed to provide the appropriate exposition.

Lord John Russell described a proverb as the wisdom of many and the wit of one. Medical aphorisms are of the same genus though some combine both the wisdom and wit of one. English medical literature is rich in these terse embodiments of clinical experience, witness the works of Gee and Horder. In Part IV of this book Dr Beaumont adds to them in what he deprecatingly labels " Idle thoughts ". The practitioner who acts on these precepts will surely raise his standards.

This is not a book which is likely to be read from cover to cover, but every doctor should possess it, so that in his leisure moments he may dip into it and gather some of the many fruits it has to offer.

Henry Cohen

Clinical Methods. A Guide to the Practical Study of Medicine

Robert Hutchison & Donald Hunter. Twelfth edition, revised with the assistance of R. R. Bomford. London : Cassell & Co. Ltd., 1949. xv + 484 pages ; 27 plates ; 101 figures. 19 × 13 cm. 17s. 6d. [£0.875]

(i) Case-taking ; (ii) general condition and appearances ; (iii) the alimentary system and abdomen ; (iv) the circulatory system ; (v) clinical examination of the blood ; (vi) the respiratory system ; (vii) the urine ; (viii) the skin ; (ix) the nervous system ; (x) examination of the eye, ear, throat and nose ; (xi) locomotory system ; (xii) clinical examination of children ; (xiii) examination of pathological fluids ; (xiv) bacteriological investigations. Appendix. Index.

This work has already weathered the supreme test of time, for it is now more than 50 years since the 1st edition appeared. This present 12th edition, under the combined authorship of Sir Robert Hutchison and Donald Hunter, assisted by R. R. Bomford, has been set up in a different format. The new size and shape makes it an altogether easier volume to handle than its predecessors, which had become too bulky. The standard of printing, however, still compares unfavourably with that of the pre-war editions ; post-war shortages and difficulties in the printing trade have not, apparently, been cured yet. On the other hand, most of the diagrams and photographs are very clear, while the newly-prepared colour plates of blood diseases and parasites are extremely well done.

As a practical guide to diagnosis and as a book which underlines the necessity of adopting a systematic scheme for taking notes and carrying out the examination of the patient, there can be no doubt that *Clinical methods* stands in a class by itself. The section dealing with the nervous system, recently rewritten by Dr Henry Wilson, is particularly impressive in its conciseness and comprehensiveness. The section on the clinical examination of children might have included a brief summary of the " milestones " of the average healthy child, for example the times of dentition, ages of crawling and walking, age of beginning speech, and so on ; while that dealing with the circulatory system seems to suffer by too much reliance on old diagrams. A little more attention might have been paid to the importance of the cardiac sounds, the changes in cardiac outline, and the interpretation of blood-pressure readings. It would perhaps have been preferable to place more emphasis on the importance of the heart muscle itself rather than upon the distinguishing characters of the various murmurs.

The disadvantages of this book are of minor importance in comparison with its fund of valuable and concise information. Like its predecessors, this edition can be regarded as a thoroughly sound investment.

R. Cove-Smith

British Pharmaceutical Codex 1949

Pharmaceutical Society of Great Britain. London: Pharmaceutical Press, 1949. xxv + 1,562 pages. 23 × 16 cm. £3 3s. [£3.15]

Part I. General monographs. Part II. Antisera, vaccines and related substances. Part III. Preparations of human blood. Part IV. Surgical ligatures and sutures. Part V. Surgical dressings. Part VI. Formulary. Part VII. Appendices. Index.

This is the fifth *British Pharmaceutical Codex*—the first appeared in 1907—and these five volumes with their addenda constitute a remarkable record of the developments of pharmacy, pharmacology and therapeutics in the past half-century. The book has grown in spite of regular, if hardly rigorous, pruning. The new volume contains 200 pages less than the last edition (1934), but has a good deal more to a page, and the avoidance of heavy type in the text adds to its dignity. It is much more than a book of reference "for those engaged in prescribing and dispensing medicines"—one might insert "and studying" after "prescribing and dispensing"—and much more than a useful supplement to the *British Pharmacopoeia* (B.P.), with which it has maintained a close and very friendly alliance. It spreads its net more widely to include 43 monographs on antisera, vaccines and related substances; nine monographs on preparations of human blood; two monographs on surgical cat-gut; 57 monographs on surgical dressings, including plasters. It also lists drugs, such as sulphapyridine, which though dropped from the B.P. may still be the better for a standard, and, appearing a year after the B.P., anticipates the promised B.P. Addendum in providing monographs on many new remedies. The present volume covers 450 extra-pharmacopoeial drugs for which it provides admirable standards, including really important advances such as dicophane (DDT), dimercaprol (BAL), folic acid, oxophenarsines (arsenoxides), proguanil ("paludrine"), propamidine and stibogluconate (a quinquevalent antimonial). Each monograph supplies a brief but admirable summary, "Actions and uses"; this is the feature which appeals alike to the busy doctor and the medical student, and makes the *Codex* their guide o choice.

There is of course room for opinion on what should be dropped and what retained. Some of us would spare yohimbine and hydrastine (and anything else of which its monograph asserts "its effect is very doubtful"), together with some at least of the four salts of lithium and the seventeen preparations which contain strychnine. These might join apocynum, betel and the rest in the pages summarizing deleted monographs. Perhaps the present delays between the completion of a text and its printing account for the absence of details on the antihistamines, the newer antibiotics, and the newer preparations of penicillin. Are we justified in allowing the romance of bygone pharmacy to linger on in "Rosae Petalum" and in "Rubi Idaei Folium" with its "water-soluble principle of unknown composition"? Must so many Latin titles continue indefinitely? We are mercifully spared them for blood products and surgical ligatures, but are faced with "Curatio Normalis I–XV", "Rayon Oleatum" and so forth as dressings.

The monograph on barbitone deals briefly with the barbiturates as a class. These drugs, other than barbitone and to a less extent phenobarbitone, are not "largely excreted in the urine"—at any rate unchanged. In the light of recent figures, phenobarbitone is not "even slower in onset and more prolonged in action than barbitone," nor would we call hexobarbitone, as distinct from intravenous injections of its sodium salt, "ultra-short-acting". Seconal sodium, recently given the approved name of quinalbarbitone, a very widely used barbiturate, is not mentioned. Strychnine sounds a very poor substitute for picrotoxin in the treatment of poisoning with the long-lasting barbiturates.

It is curious to find no reference in the "Action and uses" section for stilboestrol to its remarkable modification of prostatic neoplasms, although this receives notice in the shorter monographs on stilboestrol dipropionate, dienoestrol and hexoestrol. There are admirable monographs on heparin and dicoumarol, but no discussion of protamine as an antidote to heparin.

But these are minor points. The 1949 *Codex* is described by its publishers as "authoritative, up-to-date and indispensable". To none of these adjectives could the most carping critic take exception. He might add "remarkably comprehensive and frequently fascinating" and congratulate the Council, its Press, its Editor, its Codex Revision Committee and seven Subcommittees on a grand job, well done. October 1949 saw a first impression of 20,000 copies. A second impression was soon called for and appeared within four months. Such sales, at three guineas per copy, speak more eloquently than mere words.

A. D. Macdonald

Pocket Prescriber and Guide to Prescription Writing

David Mitchell Macdonald. Fourteenth edition, revised by Alistair G. Cruikshank. Edinburgh: E. & S. Livingstone Ltd., 1949. xv + 275 pages. 10 × 7 cm. 4s. 6d. [£0.225]

Introduction. (i) Some points in practice; (ii) some points in prescribing; (iii) incompatibilities; (iv) synonyms for drugs and medical preparations; (v) index to prescriptions; (vi) prescriptions for diseases; (vii) diets; (viii) selected national formulae; (ix) some modern remedies; (x) administration of sulphonamides; (xi) penicillin; (xii) posological tables—adults; (xiii) posological tables—children; (xiv) enemata; (xv) vitamins; (xvi) average body weights; (xvii) incubation periods; (xviii) poisoning: emergency antidote case; (xix) D.D.A. regulations.

This new edition, the 14th, of the *Pocket prescriber* is likely to retain its pre-eminent position as a vade mecum for young practitioners and students. Older physicians may regret the absence of some of the more elegant prescriptions found in previous editions, but the limitations of war-time prescribing are bound to have their repercussions on a volume of this kind.

Some rather arbitrary selections have been made from the National Formulary, and it is interesting to note that there is a woeful absence of satisfactory tonics in the list; this, however, is a defect appertaining to the Formulary itself rather than to this volume. The list of modern remedies is large and reasonably comprehensive, while together with the section on proprietary preparations it provides a useful summary of official and non-official therapeutics in a compact form. Is it a comment on our modern life that, in comparison with one of the pre-war editions (say the 10th), this volume contains no specific prescriptions for aneurysm, alcoholism, nor chlorosis?

The section on blood diseases seems a bit scanty, but that on the circulatory system is more satisfactory. That on prescriptions for respiratory diseases is more fully done, but none the less it occupies only eight pages in contrast with the fifteen pages occupied in the 10th edition; chemotherapy and the use of antibiotics have modified the necessity for exhibiting additional local therapy.

The neat sections, "Points in prescribing" and "Incompatibilities", form an invaluable opening to this little volume, while the classification of prescriptions under an alphabetical list of diseases is a helpful form of reference. Apart from the poorer type as compared with previous editions, which seems inescapable in modern book production, this handy volume can be thoroughly recommended.

R. Cove-Smith

Diabetes and its treatment

Joseph H. Barach. New York: Oxford University Press; London: Geoffrey Cumberlege, 1949. xviii + 326 pages; 2 plates; 73 figures. 24 × 16 cm. £2 10s. [£2.5]

(i) History of the disease; (ii) description of the disease and its background; (iii) clinical diagnosis; (iv) laboratory diagnosis; (v) clinical pathology, complications, and their treatment; (vi) diseases of the extremities; (vii) general surgery in diabetes; (viii) diabetic coma and its treatment; (ix) pregnancy in the diabetic; (x) diabetes in childhood; (xi) diabetes of old age; (xii) prevention and prognosis of diabetes; (xiii) treatment; (xiv) principles of diet; (xv) insulin; (xvi) continued control of the disease and patient. Diet section. Index.

The shy smile of Banting greets us from the first page of a book dedicated to his memory by a worker privileged to use insulin since the early days of its trial.

In writing for the general medical man, Dr Barach justifies his own belief that "The study of diabetes is broad and deep enough to absorb the capacities of the physician without cramping his point of view or narrowing his medical horizon." The depth of study is illustrated by the details of description and treatment. An interesting survey of the incidence and severity of diabetes in China as compared with America shows the breadth of the horizon.

For the assessment of neurovascular disease, the author describes the use of the skin thermometer, oscillometry and his own method of evaluating vibration sense. He shares the enthusiasm of Katz for the use of intravenous ether in the relief of pain due to peripheral vascular disease, but with some reservations, and notes that cases of established gangrene are not improved by this treatment.

The treatment of diabetic coma is very fully described. The recommended use of depot insulin, together with hourly doses of soluble insulin, in the treatment of ketosis, will not find favour with those physicians who prefer to observe the measurable effect of

soluble insulin on the blood and urine tests at four hours after each injection. The social embarrassments of the insulin reaction are trenchantly told and all insulin diabetics will agree that every officer of the law should know the effects of hypoglycaemia so clearly described for him in a special section.

Recent advances in diabetes tend to outstrip the literature. The clinical impression of a woman in the " prediabetic state ", who developed diabetes after the delivery of a large baby, is amply confirmed by recent work which finds no mention.

Three insulin syringes are illustrated in fig. 62, with appropriate graduations for each separate strength of insulin. In England, the use of a standard syringe graduated with 20 marks per ml. for use with all strengths of insulin is much preferred.

A large part of this book is given over to 317 separate diets to suit all circumstances of the diabetic life. It is surprising that each diet consists only of three main meals, for most insulin diabetics need buffers of carbohydrate between meals if insulin reactions are to be avoided. The diets demand the measurement of all foods. In Europe, those diabetics who have learned to measure only carbohydrate and to take such protein and fat as are allowed by rationing would find it difficult to revert to so cumbersome a system.

Dr Barach has written a companion volume for the use of diabetic patients. American doctors and their patients will find much of value in these books. Diabetics and doctors in other lands will be interested to see that the principles of good treatment remain the same, no matter how the details may vary according to circumstance and different ways of life.

H. Whittaker

The Clinical Management of Varicose Veins

David Woolfolk Barrow. London : Hamish Hamilton Medical Books ; distributed by Cassel & Co. Ltd., 1949. xii + 155 pages ; 58 figures. 24 × 16 cm. £1 5s. [£1.25]

(i) History and anatomy ; (ii) physiology and etiology ; (iii) pathology ; (iv) symptomatology ; (v) examination of the patient ; (vi) treatment of varicose veins by injection ; (vii) treatment of varicose veins of the long saphenous system ; (viii) treatment of varicose veins of the short saphenous system ; (ix) treatment of incompetent veins communicating between deep and superficial venous systems ; (x) complications ; (xi) thrombophlebitis ; (xii) after-care of the varicose extremity. References. Index.

This book, which is beautifully produced, deals with the latest developments in therapy and after-care of the varicose extremity.

The chapters on anatomy, physiology and pathology are adequately covered and that on the examination of the patient deals very fully with local tests by means of the tourniquet. Many of us may feel, however, that the importance of these tests has been over-emphasized by Dr Barrow. Such factors as the patient's age, occupation and general health receive but little mention, although details such as these are so important in planning any subsequent treatment.

Injection treatment is discussed along orthodox lines, but it is to be noted that the important sclerotics such as phenol and lithocaine receive no mention. On the other hand, sodium morrhuate, thought by many to be a dangerous drug, receives a favourable comment.

In the chapters dealing with operative treatment, Homans' operation, massive stripping and Linton's operation are all fully described. It is difficult to determine which of these procedures are generally adopted by the author and the indications he uses for their selection. For Homans' operation in-patient procedure is recommended and after discussing the technique the author makes the following statement : " Ligation of any pulsating vessel in this area is fraught with danger, since it is apt to be the common femoral." Surely this operation is not for the occasional surgeon and such advice, although most commendable, should hardly be necessary.

No mention is made of the valuable help to be obtained from the combined use of sclerotics and the various types of traumatizing needles; this combination provides an invaluable additional attack on the intima of the varix.

Linton's operation is well illustrated; it advocates the exposure of deep communicating veins through an incision extending from above the knee to the middle of the dorsum of the foot. For a varicose condition, which after all is a non-lethal complaint, such heroic treatment surely submits the patient to an unjustifiable risk. Likewise, the recommendation of stripping the saphenous vein from the groin to the ankle is a questionable procedure and should not be advocated as a routine one.

The chapters on the treatment of complications, such as ulceration and phlebitis, are not lucid. Ligation of the femoral vein in the treatment of ulceration receives undue prominence, whereas practical points, of such importance to the general practitioner, are in the main omitted. For example, the treatment for ulceration is but superficially described and although mention is made of many bandage supports, their correct and practical application is not dealt with adequately.

Physiotherapeutic measures are not discussed and there is no doubt that the practical approach to the subject is neglected, as shown for example in the case of two of the illustrations: fig. 38 shows a firm elastic compression bandage applied from the groin to the ankle, leaving the foot uncompressed, with a questionable fate as to its viability on the following day, and again in fig. 39 a most elaborate contraption of elastoplast squares and tape is applied to four portions of a pendulous abdomen in order to keep it out of the way of the operator. I think that a nurse's hand is all that is necessary.

The manual shows enthusiasm and interest in this fascinating subject, however, and the author is to be congratulated on stimulating our thought.

R. Rowden Foote

Cardiac Catheterization in Congenital Heart Disease

André Cournand, Janet S. Baldwin & Aaron Himmelstein. New York : Commonwealth Fund ; London : Geoffrey Cumberlege, 1949. viii + 108 pages ; illustrations. 28 × 21 cm. £1 2s. [£1.1]

Part I. The physiological methods. (i) Equipment, techniques and procedure —complications ; (ii) X-ray observations during catheterization ; (iii) characteristic patterns of the blood pressure tracings ; (iv) formulae for the calculation of systemic and pulmonary blood flow and of blood shunts. Part II. Illustrative cases. Bibliography.

In this monograph Cournand and his collaborators have summarized their probably unrivalled experience of cardiac catheterization. The book contains a short introduction on equipment, technique, procedure and complications, followed by *x*-ray plates showing the catheter in the various chambers of the heart and in the great vessels. Several examples of characteristic pressure tracings and a collection of formulae for the calculation of blood flow and cardiac output precede the main part of the book which deals with 17 cases of congenital heart disease. For each case there are brief notes on the history, the clinical findings, the electrocardiogram (strangely enough only standard leads are shown), the *x*-ray findings, clinical diagnosis, a diagram of the anatomical conditions found, and a list of pressure readings within the chambers. These are followed by comments on the case in the light of information obtained by the catheterization.

The investigations were carried out, usually with avertin anaesthesia, on children between the ages of two months and twelve years, and the majority of cases falls into the acyanotic or potentially cyanotic group—so that in only a few was there a chance to check the catheterization findings at operation.

The steps in the procedure are adequately described, but those contemplating similar investigations would do well to heed the authors' warning that " . . . a prolonged period of training with a team, in a laboratory already in operation, is the best means of acquiring a thorough knowledge of the method ". They should not be induced by Cournand's deceptively simple instructions to embark on a procedure for which a well-organized team of physicians, radiographers and laboratory technicians, with very good radiological and laboratory facilities, is essential, and where overexposure to *x*-radiation as well as excessive blood-loss must be avoided.

The technique described in this book differs in some ways from that used in Britain. The Americans do not use heparin in the transfusion fluid, do not " cover " the procedure with penicillin, do not collect blood samples under paraffin, and apparently prefer the saphenous or left antecubital to the right antecubital vein. They also have available a special apparatus which incorporates an electrocardiograph, an optical recorder for arterial and venous pressures, manometers for pressure readings and a reservoir for the transfusion fluid.

B. Gans

Rheumatism

H. Warren Crowe. Second edition. London: Staples Press, 1949. 270 pages; 26 figures; 6 diagrams. 22 × 14 cm. 17s. 6d. [£0.875]

Part I. Diagnosis. (i) General nomenclature and classification; (ii) general diagnosis; (iii) differential diagnosis within the rheumatic group. Part II. Pathology, morbid anatomy, and aetiology. (iv) Pathology and morbid anatomy; (v) general aetiology; (vi) the infective factor; (vii) the infecting organisms; (viii) general summary. Part III. Treatment. (ix) General considerations; (x) Charterhouse Rheumatism Clinic routine; (xi) the first interview; (xii) vaccine treatment; (xiii) hypersensitivity; (xiv) chrysotherapy; (xv) foci of infection; (xvi) local procain injections; (xvii) intra-articular injections; (xviii) medicinal treatment; (xix) physiotherapy; (xx) prognosis; (xxi) complications. Part IV. Manipulation. Part V. X-ray therapy. Part VI. Orthopaedics. Part VII. Treatment of feet. Appendix I: Laboratory technique. Appendix II: Technique of physiotherapy. Bibliography. Index.

The author's views on the rheumatic diseases are well known and he reiterates them in the 2nd edition of his book: " . . . in every case of rheumatism and arthritis there is an infective factor " and " . . . whilst streptococci are probably the main cause of osteoarthritis and non-articular rheumatism, staphylococci are predominant in rheumatoid arthritis ". His claim is that the most effective form of treatment is by vaccine which has been so standardized as to be " almost automatic in its application ", with " no excuse for its non-employment ".

Because of these claims this book deserves serious study, for if they can be substantiated then a very real advance has been made in the treatment of the rheumatic diseases. The main bulk of the evidence is, however, not statistical at all and rests largely on statements of successful treatment with vaccine by the author and others, e.g., " The difference was as conclusive as clinical trials can be ". Control series are attacked on ethical grounds since the success of vaccine treatment is considered to be established without them, and to substitute for a treatment that one " knows will do good " a " psychological procedure one knows will not " is therefore unjustified. This is despite what the author calls " bitter opposition " to vaccine therapy. The meagre statistics given are difficult to assess since they are uncontrolled, no criteria for diagnosis are given, and the methods of assessing progress are not described. His claim of a 100 per cent rate of cure for rheumatoid arthritis if treated in the prodromal stage is not, of course, susceptible of proof. None the less, on such extremely important matters it is a great disappointment to find insufficient evidence on which a judgement can be made. The importance of considering the natural history of disease, or the significance of pregnancy and jaundice remissions, is not stressed.

The pathological tests described are unique and they find no place in general medicine, so that the value of their interpretation is difficult to determine. They are apparently quite empirical. The " M " test which is a " direct measure of liver dysfunction ", " the differential sedimentation rate " and the " pathogen selective culture method " are all said to be important, but there is no yardstick by which their reliability can be assessed and their value must remain unproven.

Although this is a second edition, the references to the literature are mainly for the 1930–40 period and there is little to indicate recent advances in, for example, the endocrine aspects of the rheumatic diseases. It is unfair to criticize in a textbook the absence of references to very recent work, but it is surprising that there is no reference to Selye's work.

This book should be read by all those with a special interest in the rheumatic diseases since it lays bare the fundamentals on which the modern focal sepsis and infective theory of rheumatic diseases is based. The argument is developed by one of the chief protagonists of this concept and this book presents his ideas in a most convincing manner. The value of these theories can be assessed by each reader for himself. It is hardly suitable reading as a textbook of rheumatism since it gives only one point of view, which, as the author is the first to recognize, is not yet universally accepted. The book therefore tends to have a somewhat propagandist character, which is revealed by his plea that the " unprejudiced reader " should agree with his views, this presupposing that disagreement amounts to prejudice.

The sections on orthopaedics, manipulation and physiotherapy are less important and less controversial, and there is a small section on the care of the feet.

W. S. Copeman

The Rheumatic Diseases

G. D. Kersley. Third edition. London: William Heinemann Medical Books Ltd., 1950. xiii + 143 pages; 26 plates. 22 × 15 cm. 15s. [£0.75]

(i) Introduction; (ii) the rheumatic diseases, their etiology and inter-relationship; (iii) endocrinology and histochemistry in the rheumatic diseases; (iv) rheumatic fever; (v) rheumatoid disease, Still's disease and climacteric arthritis; (vi) specific infective arthritis; (vii) conditions simulating arthritis; (viii) osteoarthritis; (ix) spondylitis; (x) gout; (xi) fibrositis; (xii) sciatic pain; (xiii) special treatments. Bibliography. Index.

The 3rd edition of Dr Kersley's well-known little book entitled *The rheumatic diseases* remains essentially a guide for the practical clinician, although there has been added a new chapter incorporating a discussion of the adrenal cortical hormones and a short disquisition on connective tissue chemistry. These additions and the page on the adaptation syndrome of Selye will prepare the enquiring clinician for the complexities of the future, although at the moment it is not clear where many of these theoretical considerations impinge on practice.

After a general review of the etiological interrelationships of the various rheumatic diseases, each of the more common syndromes is considered in turn, starting with rheumatic fever, and followed by chapters on rheumatoid arthritis, specific infective arthritis, various simulating conditions, osteoarthritis, spondylitis, gout, fibrositis and sciatica. The many misprints will doubtless be corrected in ensuing editions (e.g. the omission of " no " on page 18, line 6, is misleading, as is the transposition of the legends to figs. 3 and 4). Especially recommended are the 30 pages on special treatments, which together with the sections on treatment under each particular disease entity constitute, in the reviewer's opinion, the most valuable feature of the book. If the sound information already available on the treatment of chronic rheumatism were to be applied in general practice it would mean a very considerable lessening of the " rheumatism problem " as seen in hospital outpatient departments.

E. G. L. Bywaters

Tuberculosis. Estudio de la Lucha Contra esta Enfermedad en España (1939-1949)

Bartolome Benitez Franco. Madrid: Patronato Nacional Antituberculoso, 1950. 497 pages; illustrations. 25 × 19 cm.

(i) Generalidades; (ii) el problema sanitario-social de la tuberculosis; (iii) epidemiológia de la tuberculosis; (iv) bases tecnicas de la lucha antituberculosa; (v) organización de la lucha antituberculosa; (vi) servicios antituberculosos provinciales; (vii) servicios antituberculosos ajenos al Patronato Nacional Antituberculoso. Apendice legislativo.

Ten years of intense activity in the anti-tuberculosis campaign in Spain justify a review of the results in an objective and unbiased manner.

Despite the high hopes placed throughout the world on B.C.G. vaccination and antibiotic therapy, the outstanding feature in the treatment of tuberculosis continues to be the shortage of beds in sanatoria. In Spain, large sums of money have been devoted to building sanatoria provided with up-to-date facilities, strategically situated and tending towards the concentration of beds in a single large building; yet still more are needed. There is also a need for more dispensaries. These fulfil a different function from sanatoria: in the dispensary the emphasis is on the community and in the sanatorium it is on the individual; medical officers in charge of one should not take part in the work of the other. Although prophylaxis is the more important of the two problems, the expense of the sanatorium is much greater than that of the dispensary. Centres of research, laboratories, teaching centres, etc. have also been built, but the reviewer feels that more emphasis should be placed on the creation of preventoriums for children with minimal lesions and of colonies for child contacts. It is necessary always to keep in mind possible improvements in organization and in methods of dealing with the problem of tuberculosis.

The anti-tuberculosis campaign in Spain is sponsored by the National Antituberculosis Patronate and by private organizations. This book contains valuable statistical data and complete information on the dispensaries and sanatoria in existence.

A. J. Coello

Laringoceles

Roberto Maisonnave. Buenos Aires: "El Ateneo", 1947. 223 pages; 65 figures. 23 × 16 cm.

Part I. (i) Desarrollo de la laringe; (ii) anatomía de la laringe, con nociones de anatomía comparada y fisiología; (iii) los sacos aereos de los animales. Part II. Los laringoceles. (iv) Sinonimia—historia; (v) etiología; (vi) patogenia; (vii) clasificación; (viii) sintomatología; (ix) diagnóstico—pronóstico—tratamiento; (x) los falsos laringoceles—analogía entre los laringoceles y los sacos laringeos de los animales; (xi) observaciones personales; (xii) conclusiones—casuistica—bibliografía.

To the laryngologist laryngocoeles are of comparative rarity, and few of us have the opportunity of seeing more than a handful in a clinical lifetime. In consequence, a monograph on this subject, incorporating previously reported cases from the world literature, together with the experiences and personal cases of an author who has spent a great deal of time and thought in the study of this subject, is of great value, and is a welcome addition to the bookshelves of the reference library.

This volume, which bears the imprint of 1947, was originally written as a thesis for a doctorate and has been received for review only recently. In all it comprises some 223 pages of text, and the subject-matter falls naturally into, and is arranged in, two main sections. The first deals with the development and the human and comparative anatomy of the larynx, and ends with a succinct account of the air sacs of animals, including their functions; the second part comprises a full account of laryngocoeles—the history relating to this condition, the etiology, pathology, classification, symptoms, diagnosis, prognosis and treatment. The subject-matter is very well presented, set out clearly, and well illustrated.

To the reviewer, the most valuable section of this monograph is that which deals with the eight personal cases which are recorded. The case histories are illustrated by some very beautiful and instructive reproductions of *x* rays, tomographs and photomicrographs, etc. The value of good tomography in the investigation of these cases is well brought out by the author's illustrations. Of the author's cases, the youngest was aged 34 and the oldest 58, the majority being in the 45 to 55 age bracket. No less than four cases were associated with carcinoma of the larynx, an incidence rate of 50 per cent!

The monograph ends with an analysis of cases reported by various authors. Of 50 ventricular laryngocoeles 10 occurred in women (20 per cent), whereas of eight extra-ventricular laryngocoeles only one was in a female. The youngest case reported was aged two years, the oldest 72. Sixteen per cent of ventricular laryngocoeles were bilateral.

The bibliography numbers no less than 111 separate references, and these should prove invaluable for the future study of this rarity. The volume is well printed, and the publishers deserve high praise for the quality of the reproductions. However, it is a great pity to see an otherwise excellently produced book spoilt by its paper cover. One would have thought that the volume deserved a better binding.

This monograph can be recommended to all who are especially interested in the subject, and it should find a place in all medical reference libraries.

F. Boyes Korkis

The Vitamins in Medical Practice

J. Shafar. London: Staples Press. 1949. 9 + 383 pages. 22 × 14 cm. £1 5s. [£1.25]

(i) General and introductory; (ii) vitamin A; (iii) vitamin B_1; (iv) the vitamin-B complex; (v) vitamin C; (vi) vitamin D; (vii) vitamin E; (viii) vitamin K; (ix) vitamin P; (x) effects of cooking, canning and fermentation on vitamin content of foodstuffs; (xi) toxic and pharmacological aspects of the vitamins; (xii) beriberi; (xiii) pellagra; (xiv) adult scurvy; (xv) rickets; (xvi) vitamin nutrition in infancy and childhood; (xvii) the vitamins in pregnancy; (xviii) the vitamins and the oral structures; (xix) the vitamins in diseases of the gastro-intestinal tract; (xx) the vitamins in hepatic physiology and pathology; (xxi) the vitamins in haematology; (xxii) the vitamins in disorders of the nervous system; (xxiii) the vitamins in endocrinology; (xxiv) the vitamins in cardiovascular disease; (xxv) the vitamins in ophthalmology; (xxvi) the vitamins in relation to disorders of the skin and hair; (xxvii) the vitamins in rheumatic affections; (xxviii) the vitamins and physical fitness; (xxix) some aspects of vitamins in relation to infection; (xxx) sulphonamides and vitamins. References. Addendum. Index.

This relatively short book on the vitamins contains an enormous amount of information in a small compass. The account is written primarily from the clinical standpoint, but nothing is omitted that could have the slightest interest for the practising physician. After a general review of knowledge concerning each of the vitamins, the author discusses the syndromes of vitamin deficiency. These two sections occupy roughly half the book. The second half contains the more interesting and useful matter, for in it the author deals with the relation of the vitamins to the various specialties, such as haematology, endocrinology, rheumatology and allergy. He also gives an account of the vitamins in pregnancy and in nutrition in childhood. An addendum brings the review of the literature up to the end of 1948.

The book is written with economy of words. Proof-reading has been thorough, though the word "hesperidin" is repeatedly misspelt (p. 106), and "sulphydryl" is to be preferred to "sulphadryl" (p. 206). The account of Crandon's experiment on vitamin-C deficiency is a little misleading. There was only one volunteer (Crandon himself) and the striking feature was the minimal nature of the gum lesions. No paper of significance appears to have escaped the author's notice, but one wonders whether he is not too modest in baldly stating the opinions of others without giving an indication of his own, condemning the bad publications and stressing the good. On the occasions when his caution does desert him, the book springs to life. To sum up, one has the impression that the author's immense industry has been well worth while and that the reader will obtain excellent value for his money and a reliable account of the medical aspects of vitaminology.

S. S. B. Gilder

Massage and Remedial Exercises in Medical and Surgical Conditions

Noël M. Tidy. Eighth edition. Bristol: John Wright & Sons Ltd., 1949. viii + 487 pages; 190 figures. 22 × 14 cm. £1 5s. [£1.25]

(i) Fractures: general considerations; (ii) fractures of the upper extremity; (iii) fractures of the lower extremity, pelvis, and spine; (iv) dislocations; (v) sprains: muscle injuries: wounds and scars: burns: amputations; (vi) treatment of the after-effects of injury: stiff joints; (vii) diseases of joints, synovial membranes, and bones; (viii) diseases of the nervous system: general considerations; (ix) diseases of the motor neurons; (x) diseases of the sensory neurons; (xi) other diseases of the brain and spinal cord; (xii) lesions of the peripheral nerves; (xiii) neuritis and neuralgia. Cramp; (xiv) functional nervous diseases; (xv) diseases of muscle; (xvi) deformities of the upper and lower extremities; (xvii) deformities of the spine; (xviii) constitutional diseases; (xix) diseases of the heart; (xx) diseases of blood- and lymph-vessels; (xxi) blood diseases; (xxii) diseases of the respiratory organs; (xxiii) abdominal and pelvic conditions. Index.

The 1st edition of this excellent book appeared in 1932. Its popularity and usefulness is amply confirmed by the appearance of the 8th edition. It contains an immense amount of information concerning those medical and surgical conditions in which treatment by physical methods is likely to be of value. It is designed as a textbook for senior students, and its object is to fill the gap between the more elementary textbooks and the larger standard works on the subject. The author has achieved a large measure of success in this, but it is also a book which should find a place in the library of any physician or surgeon interested in the complete restoration of function following illness or injury. The illustrations are good. The arrangement of the material makes it easy to use as a reference book. In this edition the section on respiratory diseases has been enlarged, that on treatment of anterior poliomyelitis revised, and the treatment, by physical methods, of sciatica due to prolapsed intervertebral disk is described.

The task of revising a book which includes notes on etiology, pathology, symptoms, and general treatment of a vast number of medical and surgical conditions must be immense. In this respect, there is room for improvement. The value of the book to students would be enhanced by the omission of certain methods of treatment no longer used, and the notes on etiology require to be brought up to date in certain sections. A valuable addition to the book would be a short section on the physiological principles underlying the use of remedial exercises. Massage in its various forms is now believed to be of less importance than the use of suitably designed active exercises.

It is certain that this book will retain the place it has won for itself as a standard work on physical methods of treatment.

J. J. R. Duthie

Proceedings of the Ninth International Congress on Industrial Medicine, London, 13th–17th September, 1948

Commission Internationale Permanente pour la Médecine du Travail. Bristol: John Wright & Sons Ltd., 1949. xxv + 1,090 pages; 25 × 19 cm. £3

Part I. Opening session, closing session. Part II. Papers contributed: (i) Industrial medicine—social aspects; (ii) industrial medicine—the environment; (iii) industrial medicine—nursing; (iv) industrial medicine—clinical; (v) industrial medicine—practice; (vi) industrial medicine—special.

This book contains the papers and discussions on scientific, technical and administrative subjects presented to the Congress which was the first to be held in Great Britain under the auspices of the Commission Internationale Permanente pour la Médecine du Travail, a voluntary association with restricted membership, founded in Milan in 1906 by 21 doctors then engaged in the practice of industrial medicine in 12 different countries. At the London Congress 43 countries were represented by delegates, and nearly 200 papers were presented. These are published in French or English, the majority in English, and each one is preceded by a synopsis in both languages.

They cover all branches of industrial medicine and are arranged in six sections. Section A comprises medical supervision; the integration of occupational health with national and community services; development of skill; incentives; job adjustment, and absenteeism. Section B deals with environment and includes studies on atmospheric pollution; building design and illumination; comfort in relation to industrial processes and climate; and applied physiology. Section C deals with the training of industrial nurses and their role in the promotion of health, and the administration of industrial nursing services in various countries.

Section D covers the clinical aspects of industrial medicine. It deals with dermatology, ophthalmology, and the etiology and treatment of surgical conditions found in industry. There is also a lecture on "The surgeon in industry", by Sir Hugh E. Griffiths. Toxicology occupies over 100 pages and includes: researches on poisons in industry, including the newer metals; their determination in the atmosphere, and the etiology, symptoms, diagnosis and treatment of industrial poisoning. The pneumoconioses considered include silicosis in various countries and pneumoconioses due to exposure to dust in coalmines and to silicon carbide, kieselguhr, tin oxide, and talc. The use of mass miniature radiography and of tomography in case-finding, diagnosis and study of pneumoconiosis are described. Inflammatory diseases of the lungs discussed, other than those mentioned, include manganese pneumonitis, fever produced by metal fumes, and bagassosis. Section E contains a description of the organization of industrial medical services, and of the lessons learned from experience in different parts of the world; this Section also has articles on hazards in special industries and in the non-productive services such as stores and transport, and on the impact on industrial health of climatic conditions, endemic diseases, and the way of life in different countries. Section S occupies the last 100 pages of the text and includes articles on very varied subjects: legal aspects of industrial medicine; training of industrial medical officers; dust control in coalmines; electrical accidents; and colour vision in industry.

It is not possible in a short review to give more than a brief outline of some of the topics included in this volume. The numerous illustrations and charts are well reproduced. The book will form a valuable record of recent work and opinion on the practice of industrial medicine in all its aspects.

E. L. Middleton

Guide to Diagnosis of Occupational Diseases

Industrial Health Division, Department National Health and Welfare, Ottawa and *Division of Industrial Hygiene, Department of Health, Ontario.* Ottawa: Minister of National Health and Welfare, 1949. 317 pages. 24 × 16 cm. 8s. 6d. [£0.425]

(i) The occupational diseases; (ii) list of occupations and their potential hazards; (iii) harmful conditions and substances; (iv) the occupational dermatoses; (v) workmen's compensation in Canada. Selected bibliography. Index.

During the last ten years the growth of Canadian industry both in size and diversity has been phenomenal. As was to be expected this rapid expansion produced problems similar to those experienced in other modern industrial communities. Canada however had the great advantage of being able to learn from the mistakes of others and in the field of industrial medicine this opportunity has not been missed. Divisions of Industrial Health have existed for some years and their activity may be judged from this book which is the result of collaboration between two of these departments. It is not a textbook—such was not the intention of the authors—but a concise and readable reference manual suitable for a wide variety of readers.

The authors rightly take the view that the control of the working environment and the supervision of the health of the industrial worker demand the co-operation of a variety of people—industrialist and worker, engineer and chemist, industrial doctor and nurse—all of whom need some knowledge of the health and safety problems introduced by changing industrial processes. But it is not only those who are closely associated with industry who must have this knowledge; the general practitioner and the medical consultant have an important part to play, for it is often they who first encounter in their consulting rooms the patient suffering as a result of working conditions. In other words, any doctor who practises in a modern industrial community must have some acquaintance with occupational disease and must know where he can find the facts he needs. Hitherto there has been no ready source giving this practical information: this book goes a long way to provide it.

One great difficulty for the general practitioner or consultant, unfamiliar with industry, is to know what hazards are associated with particular occupations. He is unlikely to know for instance that bookbinders might come in contact with acrolein, arsenic and lead and their compounds, methyl alcohol and oxalic acid, nor is he likely to know the hazards of the metal scourer or refrigerator man. The authors wisely devote an early chapter to a comprehensive list of occupations and their potential hazards; the next 200 pages (two-thirds of the book) then deal with these hazards and their manifestations. Harmful chemicals for instance are described under the following headings: properties, uses, portals of entry, physiological action and toxicology, signs and symptoms. There follows an important section on industrial skin disease; this is also accompanied by a list of the irritants likely to be encountered in various occupations. A short section on Workmen's Compensation is included, and while this has no practical value to the British doctor it is not without interest to him.

One who wishes to delve deeply will perhaps be disappointed to find that no references are given. This is a handicap for the student but for the busy practical man for whom the book is written it is not a serious drawback. The very brief space allotted to silicosis and the various other dust diseases is a more serious criticism. The book is, however, intended to be only a guide and those seeking fuller information on the pneumoconioses will have little difficulty in finding it.

Industrial medicine is growing rapidly and in this country it is paying more and more attention to the less tangible health problems of the working group. This is right and it is important that medicine should take this broad view, for only so can it make its full contribution to the health of an industrial community. Nevertheless it cannot afford to neglect the smaller but more obvious problem of occupational disease—this must be the first concern of industrial medicine. With the growing complexity of modern industry it is not easy even for the industrial physician to keep fully abreast of technical changes and this book will prove of great value to him. It is to be hoped that it will be kept up to date and will be widely circulated outside Canada.

R. E. L.

Industrial Toxicology

Lawrence T. Fairhall. Baltimore: Williams & Wilkins Co.; London: distributed by Baillière, Tindall & Cox, 1949. xi + 483 pages. 24 × 16 cm. £2 6s. 6d. [£2.325]

(i) Inorganic substances; (ii) carbon compounds. Index.

A book of reference on industrial toxicology is a need which has been sorely felt not only by specialists in occupational medicine, but also by general physicians. The chances of any doctor meeting a clinical problem due to an occupational hazard are far greater today than ever before.

The arrangement of the sections in *Industrial toxicology* has been made with all the clarity essential for a work of reference. The book is divided into two parts, the first dealing with the inorganic substances, the second with the organic, both in alphabetical order. For each substance, the characteristics are first given,

followed by a description of their industrial uses. The toxicity of the substance is then described and the clinical pictures of intoxication are included. The section on each substance concludes with the methods used for analysis. The first and last sections will be of most interest to the chemist and the industrial hygienist. The clinical descriptions of intoxication are brief but clear-cut, and only the most appropriate references have been given.

The general physician is often faced with the difficulty that patients are unaware of the toxic agents to which they are exposed. Although the industrial uses for each substance under discussion are adequately described, there is no way in which the toxic hazard for a particular industrial process can easily be found. This would be hard to remedy because of the great diversity of occupations involved; it could be attempted by a fuller index which would include entries under occupations and industries as well as under chemical substances.

The difficulty in the treatment of a subject so complex as industrial toxicology lies in maintaining a fair balance between well-known toxic agents and the newer substances introduced into industry, whose increasing use may present fresh occupational hazards. This balance has been successfully achieved by the author, who has the most profound knowledge of the whole field of industrial toxicology.

P. B. S. Fowler

Industrial Toxicology

Alice Hamilton & Harriet L. Hardy. Second edition. New York : Paul B. Hoeber, Inc. ; London : distributed by Cassell & Co. Ltd., 1949. viii + 574 pages. 21 × 14 cm. £2 10s. [£2.5]

(i) Diagnosis of industrial poisoning; (ii) alkalies, acids; (iii) chromium; (iv) lead; (v) mercury; (vi) arsenic; (vii) phosphorus; (viii) cadmium; (ix) antimony, metal fume fever, zinc, manganese; (x) beryllium; (xi) selenium, tellurium, vanadium, aluminum, copper, tin; (xii) nickel and other metals; (xiii) asphyxiants: carbon monoxide, carbon dioxide, the cyanides, hydrogen sulphide; (xiv) aromatic series: coal tar, benzene or benzol; (xv) aromatic series (*continued*): benzene derivatives; (xvi) aromatic series (*continued*): toluene and xylene, derivatives of toluene and xylene, naphthalene and naphthylamines, chlorinated naphthalenes and diphenyls; (xvii) aromatic series (*continued*): aniline dyes; (xviii) the petroleum, fatty, aliphatic series; (xix) chlorinated hydrocarbons, bromine derivatives of hydrocarbons, methyl iodide; (xx) carbon disulphide; (xxi) turpentine, tobacco; (xxii) synthetic rubber, plastics, welding; (xxiii) oil folliculitis; (xxiv) occupational cancer of the skin; (xxv) occupational cancer of the lung; (xxvi) occupational cancer of the bladder; (xxvii) radiant energy; (xxviii) stilboestrol. Bibliography. Index.

Dr Alice Hamilton and Dr Harriet Hardy are well known in the field of industrial medicine in every country of the world. It might be said that the name of Dr Alice Hamilton is to industrial physicians of the United States of America what that of Dr Donald Hunter is to those of Great Britain.

This book will be accepted as authoritative on its subject, and adequately covers every aspect of industrial medicine. It is not, however, an arid book of reference but throws emphasis and detail upon those subjects of which the authors have had the most personal experience. A clear but not dogmatic opinion is given on the many controversial subjects in this field, with always a fair selection of pertinent references.

A chapter is devoted to the increasingly important and fascinating subject of the possible toxic action of beryllium and its compounds. The chapter on lead is outstanding.

Every industrial physician will use this book. The general physician has often failed to accept the challenge presented by problems of industrial disease. The increased use of new substances that have been introduced so widely into industry today has made the subject seem too vast to be grasped by any but the occupational hygienist. The general physician, afraid of the complexities of toxicology, should welcome this book with its emphasis on the clinical picture of occupational disease.

The authors point out that individual susceptibility " constitutes one of the most troublesome factors in the practice of the industrial physician ". It is because of this factor that doctors specializing in every other branch of medicine may be presented with a diagnostic problem which can be solved only by a knowledge of industrial medicine. Isolated cases of industrial disease are probably presented to the general physician more commonly than they are diagnosed.

All medicine is one, and for this reason this book is recommended to all doctors, even those who practise specialties remote from the field of industrial medicine.

P. B. S. Fowler

SURGERY & OPHTHALMOLOGY

British Surgical Practice. Volumes 6 & 7

Edited by *Ernest Rock Carling & James Paterson Ross.* London : Butterworth & Co. Ltd., 1949. Vol. 6 : xxvi + 597 pages ; 303 illustrations ; 4 plates. 25 × 18 cm. £3. Vol. 7 : xxvi + 627 pages ; 339 illustrations ; 5 plates. 25 × 18 cm. £3

Volume 6 : (i) Malingering; (ii) manipulative surgery; (iii) mediastinum; (iv) melaena and blood in the stools; (v) melanoma; (vi) meninges—meningitis, acute and chronic; (vii) mouth and pharynx, malignant disease of; (viii) muscle and tendon—diseases and injuries; (ix) neck—cellulitis; (x) neck—cut throat; (xi) neck—cystic swellings of; (xii) neck—tuberculous glands; (xiii) neoplasms—innocent and malignant; (xiv) nerves—cranial; (xv) nerves, peripheral—injuries; (xvi) neuralgia—trigeminal, glossopharyngeal; (xvii) nose, nasopharynx and accessory sinuses; (xviii) odontomes and epithelial cysts; (xix) oedema—traumatic; (xx) oesophagus; (xxi) omentum; (xxii) optic nerve; (xxiii) orbit—injuries, infections, neoplasms; (xxiv) orthodontics; (xxv) orthodontics—surgery of; (xxvi) orthoptic training; (xxvii) ovary; (xxviii) oxygen therapy; (xxix) pain—causalgia; (xxx) pancreas; (xxxi) paralysis—management of; (xxxii) parathyroid gland—diseases; (xxxiii) pellagra; (xxxiv) pelvic organs—displacement; (xxxv) peptic ulcer and its complications; (xxxvi) perforating ulcer of the foot; (xxxvii) peritoneum and peritonitis. Index to Vol. 6.

Volume 7 : (i) Pharyngeal diverticula; (ii) physiotherapy; (iii) physique, body build and posture; (iv) pituitary tumours; (v) plastic surgery—corneal grafting; (vi) pleura—diseases of; (vii) poliomyelitis; (viii) polycystic disease; (ix) post-operative gangrene; (x) pregnancy—surgical intervention during; (xi) prostate; (xii) protracted illness—management and rehabilitation; (xiii) pulmonary abscess; (xiv) pulmonary tuberculosis; (xv) pylephlebitis; (xvi) pyloric stenosis of infants; (xvii) rabies; (xviii) radio-active isotopes; (xix) radiotherapy; (xx) reconstruction of the ear and nose; (xxi) rectum—benign tumours of; (xxii) rectum—carcinoma; (xxiii) rectum—haemorrhoids; (xxiv) rectum—proctitis; (xxv) rectum—prolapse; (xxvi) refrigeration anaesthesia; (xxvii) resuscitation; (xxviii) retina; (xxix) sacro-coccygeal region—surgery of; (xxx) salivary glands; (xxxi) scalp and skull; (xxxii) schistosomiasis; (xxxiii) sciatica; (xxxiv) sclera; (xxxv) scurvy—masked and manifest; (xxxvi) skin—diseases of, in relation to surgery; (xxxvii) speech therapy; (xxxviii) spinal column; (xxxix) spinal cord. Index to Vol. 7.

The 6th and 7th volumes of this excellent work maintain the high level of the preceding volumes.[1]

Volume 6 contains an excellent article by Sir Stanford Cade and Mr Stanley Lee on malignant disease of the mouth, throat and pharynx, in which the latest views on the radium treatment of this difficult class of growth are well set out. Professor J. H. Dible contributes a short but concise section on neoplasms, and Professor R. V. Christie, in a chapter on oxygen-therapy, lays down clearly the principles on which this treatment should be based; this latter section should be read by all practitioners. We were glad to see that L. Guttmann had written the chapter on the management of paralysis, for it is a subject on which he has shed so much light. As one might expect, the account of peptic ulcer and its complications, written by Sir Heneage Ogilvie, is a clear and dogmatic exposition and makes good reading; the Petz clamp is figured but the author quite fairly states that the operation of gastrectomy can be performed equally well without the clamp. We believe that most surgeons in this country do not use this clamp. Mr Geoffrey Keynes writes briefly on diseases of the parathyroid glands but in such an attractive manner that he whets our appetite for more. The section on diseases of the oesophagus (by Mr P. R. Allison) is a masterly contribution, but our curiosity as to the results of oesophago-jejunostomy with resection of peptic ulcer of the oesophagus was not satisfied. There are many other excellent articles which we perused with profit; the only one which we thought needed expansion was that on odontomes.

Volume 7 contains a very varied series of articles. Outstanding are three chapters on thoracic surgery—on diseases of the pleura by Mr Holmes Sellors, on pulmonary abscess by Mr R. C. Brock

[1] For reviews of Vol. 1 see *Brit. med. Bull.* 5, 406; Vols. 2, 3 & 4, see *Brit. med. Bull.* 6, 125; Vol. 5, see *Brit. med. Bull.* 6, 116.

and on pulmonary tuberculosis by Mr C. Price Thomas. Mr E. W. Riches gives an authoritative account of diseases of the prostate and manages to preserve a fine balance on the knotty question of treatment of the enlarged prostate. There is a brief but most useful chapter by Mr J. Howkins on the very difficult problem of surgical intervention during pregnancy. The five-page article on radioactive isotopes gives the surgeon a peep into the fairyland of future possibilities, but we imagine few surgeons have much experience of these isotopes, except perhaps in thyroid disease. In the chapters on diseases of the rectum the names of Dr Cuthbert Dukes, Mr E. T. C. Milligan and Mr Naunton Morgan are sufficient guarantee to satisfy anyone. This volume also contains short articles on physiotherapy and speech therapy; this is rather unusual in a textbook on surgery but we think it is fully justified and our only regret is that these two sections are so short.

Now that this big work is approaching its conclusion we may be permitted to say how much we appreciate the achievement of both editors and publisher. There is a sense of luxury in handling these beautiful volumes and it is a pleasure to turn over the fine pages and read the clear print. Each volume is a mine of up-to-date information and we consider the series the best-edited and best-produced volumes on surgery which have ever been published in this country.

V. Zachary Cope

The Comparative Anatomy and Physiology of the Larynx

V. E. Negus. London : William Heinemann Medical Books Ltd., 1949. xvii + 230 pages ; 191 figures. 25 × 18 cm. £1 10s. [£1.5]

(i) Evolution of the larynx ; (ii) modifications for olfaction ; (iii) modifications for respiration ; (iv) specialized mechanisms of respiration ; (v) function of movements at the glottis during respiration ; (vi) modifications for deglutition ; (vii) regulation of intra-thoracic pressure ; (viii) the purposive use of sound in relation to the sense of hearing ; (ix) employment of sound as a means of communication ; (x) the mechanism of phonation ; (xi) the anatomy of the human larynx. Appendix I : observations on the evolution of man from the evidence of the larynx. Appendix II : Evolution of the speech organs of man. Appendix III : Observations on Semon's law. Index of illustrations. Index.

In 1929 Mr Negus published *The mechanism of the larynx*, a monumental work founded on his extensive researches into the comparative anatomy of the animal kingdom. This present volume is a condensed version and is strikingly successful, an epithet that cannot be applied to all similar ventures.

This is a book which should be familiar to all laryngologists, and it could also be studied as a model by all who intend to carry out research on other parts of the body. It is full of information and is founded on an extensive and detailed study of a very large number of animals. Beginning with fish that for one reason or another were compelled to spend part of their existence on land, and therefore had to develop an air-breathing apparatus, the author shows how the primitive opening into the "lung" gradually becomes more complicated till it develops into the highly specialized organ in man.

The author then discusses how modifications in the structure of the larynx have depended on various functions; for example, in Chapter II he describes the structural modifications caused by the needs of olfaction, and in Chapters III and VI respectively he describes the adaptations of the laryngeal structure to meet the functions of respiration and deglutition.

There are great differences in the need for a sense of smell among various creatures. Reptiles and birds have a poor sense of smell, while mammals have a strong olfactory sense because they must be able to draw air through their noses even while feeding. For this reason a flap, the epiglottis, is found closing the gap between the nasopharynx and larynx. In some other mammals which rely more on sight than smell. the epiglottis and palate are not in contact ; the epiglottis is therefore largely connected with the sense of smell. All these points are illustrated with appropriate drawings, and at the end of each chapter the author summarizes his conclusions. In the chapter on respiratory modifications it is pointed out that the glottis serves to some extent as an obstruction to the passage of air to the lungs ; free entry of air is highly important for those animals that rely on fleetness of foot to escape their enemies, and the glottis is modified accordingly. The glottis in woman is only 52 per cent of the area of the trachea. Air sacs are developed to improve respiration and not voice.

In the chapter on modifications for deglutition the author describes how lateral food tracts are developed so that food cannot inundate the larynx ; the epiglottis, as it were, directs the stream. The larynx, too, is raised during the act of swallowing and the function of the cartilage of Santorini in helping to open the oesophagus is clearly explained. (Slight confusion might occur in the interpretation of fig. 166, owing to the misplacement of an arrow in one of the illustrations.) Other chapters, all most illuminating, deal with the regulation of intrathoracic pressure, the purposive use of sound in relation to the sense of hearing, sound as a means of communication, the mechanism of phonation, and the anatomy of the human larynx.

Perhaps the most interesting suggestion is that those animals which use their fore-limbs for strenuous efforts (climbing, lifting, etc.) are able to fix the chest ; to do this the glottis is constructed so that air can be held in the lungs, thus constituting a "valvular" larynx. This valvular function is present in man ; sudden closure of the glottis can be observed, for example, when an effort is made to close a spring balance between the hands.

The work is profusely illustrated, the numbers of the illustrations corresponding to those of the collection of specimens in the Royal College of Surgeons—an admirable arrangement. The majority of the pictures are skilful drawings, by Mr Steward and Mr Tompsett, of preparations by the author. There are also several spirited sketches by Mrs Negus of a diversity of animals ; they are in characteristic attitudes in order to demonstrate important points in the author's deductions relating habit to laryngeal structure.

W. M. Mollison

The Anatomy of the Eye and Orbit, Including the Central Connections, Development and Comparative Anatomy of the Visual Apparatus

Eugene Wolff. Third edition. London : H. K. Lewis & Co. Ltd., 1948. viii + 440 pages ; 323 figures. 25 × 19 cm. £2 5s. [£2.25]

(i) The bony orbit and accessory sinuses of the nose ; (ii) the eyeball ; (iii) the appendages of the eye ; (iv) normal appearances as seen with the slit-lamp and corneal microscope ; (v) the extrinsic muscles of the eye ; (vi) the nerves ; (vii) the visual pathway ; (viii) the vessels ; (ix) the development of the eye ; (x) comparative anatomy. Index.

This beautifully produced edition has been thoroughly revised and more than 80 illustrations have been added, of which the majority are drawn from the author's own preparations.

The main changes are in the descriptions of the ciliary muscle, the substantia propria of the cornea, the vitreous, the zonule of Zinn, the distribution of the lacrimal fluid, the muco-cutaneous junction at the lid margin, the precorneal film. the retinal capillaries and the central connexions of the visual apparatus.

The text contains all that is currently acceptable in the teaching of ophthalmic anatomy in this country, and the facts are presented in an attractive and lucid manner which makes this book especially readable.

P. Griffiths

The Practice of Refraction

Stewart Duke-Elder. Fifth edition. London : J. & A. Churchill Ltd., 1949. xiv + 317 pages ; 216 figures. 21 × 14 cm. 18s. [£0.9]

(i) Introductory ; (ii) refraction ; (iii) accommodation and convergence (iv) the muscle balance ; (v) clinical methods ; (vi) spectacles. Appendices.

This edition contains the first thorough revision of the text since the 3rd edition appeared in 1938. Owing to the exigencies of war, the 4th edition was little more than a reprint of its predecessor.

The character of the book is unaltered but additional material has been included on refraction, aniseikonia, mechanism of accommodation, anomalies of convergence, orthoptic treatment of muscular imbalance, streak retinoscopy and velonoskiascopy. The chapter on the prescription of spectacles has been amplified and includes a section on contact lenses. The text is lucidly presented in as small a compass as possible and the production is in keeping with the high standard expected of the publishers.

P. Griffiths

Ocular Signs in Slit-Lamp Microscopy

James Hamilton Doggart. London : Henry Kimpton. 1949. xiii + 112 pages ; 93 figures. 24 × 16 cm. £1 1s. [£1.05]

(i) The value of slit-lamp microscopy ; (ii) technique of examination ; (iii) the normal eye ; (iv) corneal abnormality ; (v) aqueous disturbances ; (vi) pathological signs in the iris ; (vii) lenticular changes ; (viii) changes in the vitreous ; (ix) the evolution of slit-lamp microscopy of the living eye. Appendix. Bibliography. Index.

This is the only modern textbook on slit-lamp microscopy published in Great Britain ; it has had an excellent reception, as it gives an adequate and concise account of practical and essential facts.

A short book on biomicroscopy like this one has been needed for some time. The author, by curtailing descriptions of apparatus and by omitting unimportant details, has written a book of the right length which is also very readable. Both undergraduate and postgraduate students will find it extremely useful. If they want more detailed information they can read the large treatise of M. L. Berliner (*Biomicroscopy of the eye*, New York, 1943) and the three volumes by Alfred Vogt (*Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges* : vols. 1 and 2, Berlin, 1930–31 ; vol. 3, Zürich, 1941).

The quality of the colour plates is excellent and the publishers are to be complimented on the high standard of production.

P. Griffiths

OBSTETRICS & GYNAECOLOGY

Stillbirths : their Epidemiology and Social Significance

Ian Sutherland. London : Geoffrey Cumberlege, Oxford University Press, 1949. xii + 93 pages ; 4 figures. 22 × 14 cm. 7s. 6d. [£0.375]

(i) Introduction ; (ii) general epidemiology ; (iii) the medical causes of stillbirth ; (iv) biological factors affecting the rate ; (v) the necessity to study social factors ; (vi) social influences and the stillbirth rate ; (vii) antenatal care and other socio-medical influences ; (viii) possible further reduction in the stillbirth rate ; (ix) summary and conclusions. References. Index.

Dr Sutherland has made a comprehensive and detailed survey of the epidemiology and social significance of stillbirths, including an extensive review of the literature.

He points out that the total annual wastage of infant life in England and Wales is something of the order of 21,000 stillbirths, 17,000 deaths under 4 weeks of age, and 15,000 deaths between the ages of 4 weeks and 1 year. This is more than double the number of deaths occurring annually from pulmonary tuberculosis and is thus exceeded only by the 70,000 deaths from cancer.

There is difficulty in making comparisons of stillbirths between countries because of the variation in definition. In those countries such as Holland, Denmark and New Zealand, where comparison with Great Britain is permissible, the incidence of stillbirths is much lower than in Great Britain.

In England and Wales, before the Second World War, there was a considerable geographical variation in the incidence of stillbirths, but during the war the stillbirth rate fell steadily until 1944. From the medical aspect it would appear that antenatal influences are likely to be more improved than obstetrical factors. The quality of antenatal care is probably of greater importance than the quantity.

With regard to biological associations, stillbirths appear to be more frequent among male than female births. Dr Sutherland confirms the findings of other workers, that the stillbirth rate is more or less constant until mothers reach the age of 25. Thereafter it increases rapidly with age. The rate is higher for first births than for second births, but thereafter rises gradually. The interval between successive births also appears to have some influence. If this is either too long or too short the liability to stillbirth increases appreciably. The higher stillbirth rate is associated with a higher rate of previous loss of infants of the same mother.

The medical and biological factors, however, are insufficient in themselves to account for either the pre-war or the geographical variation, or the war-time decline.

Dr Sutherland has made a detailed study of two groups of areas, the 83 county boroughs of England and Wales and the 48 administrative counties outside London. It was found that the stillbirth rate in the county boroughs was associated with unemployment or poorly paid work, but not with overcrowding. The experience of the administrative counties broadly confirmed these findings, although the results were less clear cut.

Dr Sutherland suggests that the best policy for further reduction in the stillbirth rate appears to be to maintain the equitable distribution of essential foods, to ensure that sound education and nutrition reaches the poorest quarters of the community, and to improve the medical and obstetrical facilities available to expectant mothers.

This is a most interesting and stimulating book, and makes a number of suggestions for further detailed field studies.

Jean M. Mackintosh

Haemolytic Disease of the Newborn

M. M. Pickles. Oxford : Blackwell Scientific Publications, 1949. x + 181 pages ; 21 figures. 22 × 14 cm. 15s. [£0.75]

(i) Historical evolution of the disease ; (ii) Rh antigens and antibodies ; (iii) Rh in relation to haemolytic disease ; (iv) the mechanism of immunization ; (v) the pattern of the disease ; (vi) treatment ; (vii) sequelae of haemolytic disease of the newborn and other suggested manifestations of Rh incompatibility. Appendix. Bibliography. Index.

This book sets out to describe adequately and simply the complex story which results from incompatibility between the bloods of the mother and foetus.

The first chapter is devoted to a brief survey leading up to the identification of hydrops foetalis, icterus gravis neonatorum and anaemia neonatorum as three varying manifestations of one condition and terminating in the discovery of the inherited blood factors which caused the incompatibility. The author then describes the Rh antigens and antibodies, using both the Wiener and the Fisher-Race nomenclature. This difficult subject is dealt with excellently, the Coombs test for detecting incomplete or blocking antibodies being very clearly described. The relation of these antigens and antibodies to haemolytic disease of the newborn is next discussed. The estimation of complete and incomplete antibody in maternal serum and of the degree of cell sensitization and the amount of free antibody in the blood in the neonate in the evaluation of the severity of the disease is critically studied. These two chapters need very careful reading as much fundamental information is compressed into them.

The last part has a more clinical note. The first chapter is a brief one on the mechanism of maternal immunization. This is followed by a long chapter on the disease itself—its frequency and its manifestations. The clinical, pathological, haematological, serological and biochemical aspects are all considered in turn. The next chapter is on treatment before, at, and after birth, finishing with a very valuable summary of points to keep in mind. The last chapter is on the possible after-effects and here the critical faculty of the author is exercised in evaluating and often discounting many alleged sequelae described in the literature.

There is an appendix on laboratory techniques. This description of the methods used by the author in her laboratory is useful to a trained haematologist.

The bibliography is well chosen and covers a wide field without being exhaustive. There are only a few typographical errors and the only one which might be misleading is on page 111, line 22, where " 0.4 to 2.0 g. " should be " 0.4 to 2.0. μg. "

This is certainly a book to have and no one who has to deal with the problem of haemolytic disease should be without it. For such workers it is not a book for the bookcase but for the desk.

W. W. Payne

MEDICAL SCIENCES & RESEARCH

Recent Advances in Physiology

W. H. Newton. Seventh edition. London, J. & A. Churchill Ltd., 1949. 268 pages ; 90 figures. 21 × 14 cm. £1 1s. [£1.05]

(i) The physical basis of temperature regulations ; (ii) water diuresis ; (iii) digestion ; (iv) some aspects of the physiology of pregnancy ; (v) blood pressure and the kidneys (with I. Calma) ; (vi) catheterisation of the heart ; (vii) the electrical excitation of nerve ; (viii) cutaneous sensation ; (ix) auditory impulses ; (x) colour vision. Index.

This new edition has broken a tradition of the six that have gone before. All chapters have been rewritten and there is no longer that repetition of material which characterized the earlier editions. The author has disarmed many critics by his introductory statement that the book is not intended to contain up-to-the-minute exhaustive reviews of the subjects chosen, such minutiae being the province of the specialist reviewers and collators. Rather has he sought to present surveys of subjects which are of recent development and which would serve as an introduction and indicate the main currents of thought. In this Professor Newton has done well. The book will be of high value to all who want a balanced account of progress in some narrow aspect of physiology. Each chapter is based on reports from a few workers in each field and many of the references are to work which must be considered as classical in the literature of the problem. Such an approach will disappoint the reference-hunter while earning the gratitude of those not sufficiently versed in the literature to be able to see the wood for the trees.

The choice of subjects is wide, embracing such a variety as the detailed physiology of the nerve fibre, recent theories about colour vision, some aspects of pregnancy, the physics of heat loss by the skin, and so on. Although the author declares himself unrepentant about omissions it is inevitable that one looks for references to particular work. It should be noted, however, that the main writing seems to have been finished in 1947. Most of the literature in the references appeared before this and the few later ones (up to 1949) were probably slipped in during printing. Otherwise the reader may be puzzled not to find, for example, any reference to Lorente de Nó's symposium of his own work on the nerve fibre, which was available late in 1947. In spite of this the chapter on the electrical excitation of nerve gives a most detailed summary of the progress made in the last decade, particularly at Cambridge. In this chapter, as in that dealing with Winslow, Herrington & Gagge's method of partitional calorimetry, will be noted the increasing need for the physiologist to make his deductions in mathematical forms. The chapter on digestion includes a summary of the account given by Wolf & Wolff of their observations on the physiology of the human gastric mucosa. Their observations on that organ's sensibility to pain are unfortunately left in isolation. It would have been most valuable if the author could have related them to the other work on deep pain sensation of Lewis, Kellgren, Hardy, Wolff and others, of which these observations form an important part. The review of blood-pressure and the kidneys deals with the two aspects which make most appeal to those schooled in the disciplines of experimental physiology—namely, the work leading to the recognition and description of renin, and the account by Trueta and his colleagues of the renal shunt mechanisms. In this account the author gives prominence to the attempts made to correlate these results with the mechanism of clinical hypertension, but one might object that the clinical findings in a clinical problem deserve rather more attention than they receive ; while the very probable homeostatic role of the renin mechanism receives little mention.

In this book the author has presented discriminating and useful reviews of the literature as it appears to the non-specialist. Only in the chapter on the pregnancy syndrome is he entering his own field. It is to be regretted that, because of the recent death of Professor Newton, we shall have no more Recent Advances from his pen. To have lost such an excellent writer, whose knowledge covered so wide a field, is a sad blow to the literature of experimental physiology. Whoever may undertake the writing of future editions of *Recent advances in physiology* has been left a high standard of scholarship to attain.

C. B. B. Downman

Penicillin, its Practical Application

Edited by *Alexander Fleming.* Second edition. London : Butterworth & Co. Ltd., 1950. xiii + 491 pages ; 63 figures. 22 × 14 cm. £1 10s. [£1.5]

(i) History and development of penicillin ; (ii) chemistry and manufacture of penicillin ; (iii) pharmacy of penicillin ; (iv) pharmacology of penicillin ; (v) bacteriological control of penicillin therapy ; (vi) methods of administration ; (vii) prophylactic use of penicillin ; (viii) subacute bacterial endocarditis ; (ix) diseases of the chest ; (x) wounds and gas gangrene ; (xi) plastic surgery including burns ; (xii) orthopaedic surgery and fractures ; (xiii) osteomyelitis ; (xiv) hand infections ; (xv) abdominal infections ; (xvi) obstetrics and gynaecology ; (xvii) sepsis neonatorum ; (xviii) brain and meningeal infections ; (xix) venereal diseases ; (xx) penicillin in eye infections ; (xxi) otorhinolaryngology ; (xxii) penicillin in dermatology ; (xxiii) dental and oral infections ; (xxiv) penicillin in animal diseases ; (xxv) streptomycin ; (xxvi) penicillin sensitivity ; (xxvii) penicillin and the general practitioner ; (xxviii) penicillin in acute infectious diseases. Appendix A : penicillin resistance. Appendix B : chloromycetin and aureomycin. Index.

The 1st edition of this book appeared three years ago and the demand for a 2nd edition is evidence of its value and of the advances in knowledge and experience which have been made during the intervening period. In particular, the supply of penicillin has now become so plentiful as to be available for all needs, even trivial ones, and experience has been gained so that treatment has now become more standardized. In addition, commercial penicillin has become more pure. For all practical purposes, penicillin of good quality has now no toxicity, and such direct toxic effects as have been recorded in man have been of a minor nature ; on the other hand, various allergic reactions have been described, chiefly urticaria and erythematous-vesicular eruptions.

The book consists of a series of independent contributions written by many specialists, each an expert in his own field, showing how penicillin can best be used in the different departments of medical practice. The first or general part of the book has chapters about chemistry, manufacture, pharmacology and administration of penicillin. The emphasis is laid chiefly on the information which is needed in clinical practice and much space is devoted to the methods of dispensing and administering penicillin, and to methods of controlling penicillin by bacteriological techniques. The clinical section (which occupies most of the book) describes the application of penicillin to special sites and conditions. The surgical uses of penicillin are particularly well covered. Much of the treatment of wounds is based on military experience during the fighting in north-west Europe during the last year of the Second World War. The widespread use of penicillin for prophylaxis allowed secondary closure of wounds to be performed frequently and safely, and thus brought untold benefit in the prevention of pain and the production of better functional and cosmetic results. However, it is emphasized that no therapeutic agent can be expected to succeed unless the associated surgical treatment is adequate. Accordingly practical advice about the surgery is given as well as the directions about penicillin itself. There are separate sections dealing with osteomyelitis, hand infections, obstetrics and gynaecology and many other specialties. In affections of the ears, nose and throat, penicillin therapy shows spectacular results in the acute and spreading infections, so that the outlook in many grave conditions has been transformed. In chronic infections, however, the results of penicillin alone have not been so favourable and surgical intervention is required to remove diseased tissue and promote adequate drainage. There are also chapters describing the use of penicillin in more medical conditions, such as acute infectious diseases, dermatology and venereal diseases. As regards syphilis, the author of the chapter concerned considers that penicillin is so efficacious for early cases that the addition of arsenical treatment is unnecessary, and may even be harmful on account of its toxicity ; reinforcement by bismuth, however, is safe and desirable. Special chapters deal with sensitivity to penicillin (which appears in about 25 per cent of patients, mostly in the form of urticarial reactions), the use of penicillin in animal diseases, and streptomycin.

Throughout, the book is written for the guidance of the practising doctor, whether in general practice or in one of the specialties. Information is given mostly in dogmatic form, based on the writers' own experiences. This makes it easy to assimilate and apply. The book is convenient in size and format and is strongly recommended to all who require to prescribe or administer penicillin frequently.

F. Hawking

Evaluation of Chemotherapeutic Agents

Edited by *Colin M. MacLeod*. New York : Columbia University Press ; London : Geoffrey Cumberlege, 1949. xii + 205 pages ; figures. 23 × 16 cm. £1 8s. [£1.4]

(i) The significance of drug concentration in the blood, as applied to chemotherapy ; (ii) blood levels, renal clearance, and chemotherapeutic activity, with particular reference to arsenicals and penicillin ; (iii) the binding of chemotherapeutic agents to proteins and its effect on their distribution and activity ; (iv) the problem of microbial resistance to chemotherapeutic agents ; (v) defense mechanisms of the host in relation to chemotherapy of acute bacterial infections ; (vi) the nature of the lesion and the response to antimicrobial therapy ; (vii) transcutaneous antibiotic therapy of localized soft tissue infections ; (viii) chemoprophylaxis of meningococcal infections and of bacillary dysentery ; (ix) an evaluation of chemoprophylaxis of streptococcal infections ; (x) evaluation of antimalarial drugs ; (xi) the chemotherapy of rickettsial diseases ; (xii) chemotherapy of viral infections ; (xiii) the experimental evaluation of chemotherapeutic agents in cancer ; (xiv) the clinical evaluation of chemotherapeutic agents in cancer.

The development of chemotherapy has been so rapid and so far-reaching that it is difficult, if not impossible, to keep pace with all its more recent manifestations. It is, therefore, a wise step on the part of the Section on Microbiology of the New York Academy of Medicine to publish the symposium on certain aspects of chemotherapy which they held in the spring of 1948. Unpublished symposia are too soon forgotten but the prompt publication by acknowledged experts of extensive reviews in their particular fields of endeavour are of immense value since they bring to the attention of laboratory workers and clinicians alike a vast mass of correlated and authoritative facts. The main object of this symposium was a general evaluation of the many factors involved in the success or failure of chemotherapeutic remedies, rather than a discussion of the specific compounds used in the treatment of particular diseases.

With this end in view twelve reviews deal with such questions as the significance of drug concentrations in the blood as applied to chemotherapy (E. K. Marshall) ; blood levels, renal clearances, and chemotherapeutic agents with special reference to arsenicals and penicillin (H. Eagle) ; the binding of chemotherapeutic agents to proteins and the consequent effects on distribution and activity (B. D. Davis) ; bacterial resistance (H. E. Alexander) ; chemoprophylaxis as applied to streptococcal infections (A. T. Wilson), and to meningococcal and *Shigella* infections (F. S. Cheever). W. B. Wood deals with the role of the defence mechanisms in relation to the chemotherapy of bacterial infections ; W. McDermott discusses the nature of the lesion and the response to antimicrobial therapy. E. K. Sanders & J. S. Lockwood suggest the possible local application of antibiotics in limiting the spread of localized infections of soft tissue. The chemotherapy of virus infections, still in its infancy, is adequately dealt with by F. L. Horsfall, that of rickettsiae by J. P. Fox, while J. A. Shannon gives a résumé of the laborious investigations on antimalarial compounds with which he was so intimately associated during the war years. Finally, the chemotherapy of cancer is adequately surveyed in two admirable chapters by C. C. Stock & C. P. Rhoads who consider the experimental evaluation of chemotherapeutic agents, and by D. A. Karnofsky & J. H. Burchenal who attempt to evaluate chemotherapeutic agents in the treatment of human cancer. These two chapters are written without any intention of labouring the belief that all cancers are necessarily caused by extrinsic parasitic agents.

Where all the articles are of such high excellence it would be invidious to select any for special praise. Each section is provided with references and the book is excellently produced. Unfortunately there is no index.

G. M. Findlay

Symposia of the Society for Experimental Biology. Number III, Selective Toxicity and Antibiotics

Society for Experimental Biology. Cambridge : University Press. 1949. vi + 372 pages ; figures ; plates. 25 × 16 cm. £1 15s. [£1.75]

(i) The organic chemist's approach to chemotherapy ; (ii) the differential activity of certain anti-malarial agents against protozoa and bacteria ; (iii) the study of enzymes in relation to selective toxicity in animal tissues ; (iv) the design of bacterial inhibitors modelled on essential metabolites ; (v) antibiotics derived from *Bacillus polymyxa* ; (vi) the resins of hops and antibiotics ; (vii) systemic insecticidal properties induced in plants by treatment with fluorine and phosphorus compounds ; (viii) surface activity and permeability as factors in drug action ; (ix) the permeability of insect cuticle ; (x) selectivity of drug action in protozoal blood infections ; (xi) aspects of the selective toxicity of sulphonamides and other anti-metabolite inhibitors ; (xii) the effects of long-chain fatty acids on the growth of *Haemophilus pertussis* and other organisms ; (xiii) the effect of unsaturated fatty acids on gram-positive bacteria ; (xiv) the action of penicillin on the assimilation and utilization of amino-acids by gram-positive bacteria ; (xv) adaptation of bacteria to resist drug action ; (xvi) the significance of hydrogen-ion concentration in the study of toxicity ; (xvii) the effects of phenylcarbamates on the growth of higher plants ; (xviii) the comparative toxicity of phytocidal substances ; (xix) therapeutic interference ; (xx) some effects of diet on toxicity —the influence of diet on the induction and inhibition of tumours ; (xxi) external metabolites and ecological adaptation ; (xxii) the production of antibiotics by micro-organisms in relation to biological equilibria in soil.

This book contains 22 contributions on a very varied selection of subjects, all of which are in some way concerned with selective toxicity and modes of drug action and a few with antibiotics in the more restricted sense in which the word is generally used. The names of the contributors guarantee the authoritative nature of the contributions, but something might have been gained by restricting the symposium to a narrower field.

It is, unfortunately, impossible in a short review to discuss each contribution critically. The general impression is of the complexity of the subject, and of the little that is really known of selective toxicity and the wide field that remains for investigation. The idea of substrate competition crystallized by Fildes and Woods has released a flood of research, much of which has proved disappointing, probably because, as H. N. Rydon says ("The design of bacterial inhibitors modelled on essential metabolites"), there has not been a proper appreciation of the structural factors on which similarity between metabolite and inhibitor must be founded. Mere pictorial analogy may be misleading. The classic instance of *p*-aminobenzoic acid and sulphanilamide on which the theory was mainly based has not been followed by many analogous examples and has not borne much fruit in the way of new therapeutic agents, except in the rather remote analogy of the antimalarial drugs (mepacrine, etc.) to riboflavin. According to Rydon :

> Pictorial analogy is not enough because an analogue may look like a metabolite and yet lack the chemical groupings necessary for combination with the appropriate enzyme . . . Pictorial analogy is too much, since there may be a great deal in the structure of the metabolite which is not directly concerned in its attachment to the enzyme.

Rydon also makes the interesting suggestion that, instead of an inhibitor being modelled on the metabolite, it might equally well be modelled on the enzyme, and opens up the prospect of making synthetic peptides which may compete with bacterial enzymes for known metabolites. Certain antibiotics with a polypeptide structure, such as gramicidin, aerosporin, and, in a modified sense, penicillin, may act in this way.

A further complication is that a successful drug must possess the appropriate physical as well as chemical properties. W. A. Sexton in his contribution emphasizes that "it is usually not sufficient to examine a single member as representative of a chemical type, for a variation in physical properties might make all the difference between success and failure". The physico-chemical aspect is also discussed by A. R. Trim & A. E. Alexander ("Surface activity and permeability as factors in drug action"):

> . . . the mode of action of a particular drug can only be determined by experiment. Nevertheless, a consideration of the physical characteristics of a drug can be a useful guide to its mode of action.

Physical properties are intimately concerned in the absorption and diffusion of a drug, i.e., the problem of getting the drug to the right situation in the right condition to exert its activity. In other words, the drug must be compatible with its environment.

Physico-chemical factors appear to provide an explanation of the relative activity of different members of the sulphonamide group of drugs. Recent work on the mode of action of these drugs is described in a contribution from D. D. Woods & R. H. Nimmo-Smith, which also deals with recent work on the chemical processes for which *p*-aminobenzoic acid is required by the cell, viz. the synthesis of folic acid, purines and certain amino-acids.

An alteration in constitution which may appear slight to an organic chemist may be accompanied by an abrupt change in biological effect. An example of this is given by F. L. Rose ("The differential activity of certain anti-malarial agents against protozoa and bacteria") ; he deals with the series of compounds which led to the production of paludrine, and shows how the transition from compounds containing a pyrimidine nucleus to the acyclic diguanide (paludrine), though chemically slight, is accompanied by an abrupt change in biological action.

Sir Cyril Hinshelwood gives an interesting account of the work on drug resistance in bacteria with which he has been associated.

Since adaptation depends upon changes in the material constitution of the cell which are caused directly by the specific influence of the inhibitory drug upon various rates of synthesis, the problem is closely related to the subject of selective toxicity. The fact that certain types of cell adapt themselves rapidly to ignore the presence of one drug but seem quite incapable of acquiring resistance to another may be explained by the hypothesis that different drugs intervene at different stages of the sequence of synthetic reactions.

Adrien Albert discusses the action of foreign substances in preventing the normal curative action of a drug. The commonest and most puzzling examples of therapeutic interference are those in which the antagonists have such great similarity to one another that it has been thought impossible that they could react together, e.g. interference of parafuchsin with the curative action of acriflavine on trypanosomiasis in mice. To account for this, Albert advances a new hypothesis which supposes that the interfering substance sterically obstructs the drug from combining with a receptor by forming with it a mixed micelle devoid of toxic properties.

R. A. Peters contributes a review of the cases in which it has been convincingly shown, largely as a result of his own work, that the action of poisons is directly related to selective effects upon enzymes, e.g. the arsenical poisons and lachrymators and the fluorophosphonates. The action of mustard gas is still very imperfectly understood.

E. M. Lourie (" Selectivity of drug action in protozoal blood infections ") considers that the acquirement of drug resistance is probably explicable in physical or physico-chemical terms rather than along more strictly chemical lines. The contribution of the host's immunity mechanisms to the total chemotherapeutic effect is often neglected in considering the action of a drug on a parasite.

The remaining contributions are on more specialized subjects and of less general interest. The book is excellently produced and, though it exhibits the defects which are common to most symposia, it contains much of great interest to those concerned with the subject.

Norman Evers

Partition Chromatography

Organized and edited by *R. T. Williams*, assisted by *R. L. M. Synge*. Cambridge : University Press, 1949. (Biochemical Society Symposia, No. 3.) 103 pages ; figures. 25 × 16 cm. 6s. [£0.3]

(i) Some theoretical aspects of partition chromatography ; (ii) application of partition chromatography to the study of protein structure ; (iii) applications to study of amino-acid and protein metabolism ; (iv) partition chromatography and its application to carbohydrate studies ; (v) anthocyanins, flavones and other phenolic compounds ; (vi) partition chromatography of organic acids, purines and pyrimidines ; (vii) partition chromatography with stationary phase other than pure water ; (viii) general review of the applicability of the method. Supplementary bibliography.

In 1906 Tswett invented the adsorption chromatogram, but some twenty years were to elapse before this valuable method of separation became generally adopted. The partition chromatogram, introduced by Martin & Synge in 1941, has not suffered the same neglect. In the space of only a few years it has become very widely established ; this is particularly true for partition chromatography on paper, which was introduced by Consden, Gordon & Martin in 1944. Nowadays, hardly a week passes without some reference in the scientific journals to the application of these new methods. This is not surprising because, in addition to its simplicity, the partition chromatogram can be used for separating many substances of biological importance that cannot be dealt with satisfactorily on the older adsorption chromatogram. The appearance of the Biochemical Society's symposium on a subject of such rapid and fruitful growth is therefore welcome. This publication contains the proceedings of the Symposium held towards the end of 1948, at which seven papers by various authors were read. An introduction is contributed by Dr (now Professor) E. Baldwin, and a general review of the papers is given by Dr R. L. M. Synge. Also included are contributions to discussions of the papers. Most of the papers deal with applications to certain important families of substances. One paper, by Dr A. J. P. Martin, is concerned with theoretical aspects, and another, by Dr A. A. Levi, with modifications of partition chromatography.

In his paper, Dr F. Sanger deals with structural studies of proteins and polypeptides and shows how the new techniques have proved essential for the elucidation of amino-acid sequences. In another important field, too, namely that of polysaccharides, these methods have been used successfully for structural studies. This aspect is reviewed by Dr S. M. Partridge. Dr C. E. Dent deals with applications to the study of amino-acid and protein metabolism. Much useful information regarding certain diseases and of amino-acid and peptide content of biological fluids has been obtained by the use of paper chromatography. Another important group, comprising anthocyanins, flavones and related phenolic substances is discussed by Dr E. C. Bate-Smith. The separation and estimation of fatty acids on buffered silica gel columns and of purines, pyrimidines and related substances on paper chromatograms is reviewed by Dr S. R. Elsden. Partition chromatography, with stationary phase other than pure water, is dealt with by Dr A. A. Levi. This has already had important applications in the penicillin field and further modifications will extend chromatography to deal with important water-insoluble substances such as lipids and sterols. In the contributions to the discussion of the papers many topics are covered, some of special interest to medical workers, such as the use of radioactive tracers in chromatography, studies of metabolism of micro-organisms, separation of porphyrins and purification of the anti-pernicious anaemia factor, to mention only a few. The proceedings are admirably summed up by Dr R. L. M. Synge and he foreshadows some important developments in technique. Extremely valuable is the comprehensive and up-to-date bibliography at the end of the publication.

In little more than 100 pages, at the cost of only a few shillings, is contained a wealth of information ; there is much here that will be of interest and value to medical investigators.

R. Consden

Trace Elements in Food

G. W. Monier-Williams. London : Chapman & Hall Ltd. 1949. viii + 511 pages. 22 × 14 cm. £1 10s. [£1.5]

(i) Copper ; (ii) lead ; (iii) zinc ; (iv) tin ; (v) arsenic ; (vi) antimony ; (vii) selenium ; (viii) iron ; (ix) nickel ; (x) cobalt ; (xi) manganese ; (xii) iodine ; (xiii) bromine ; (xiv) fluorine ; (xv) boron ; (xvi) silicon ; (xvii) aluminium ; (xviii) silver ; (xix) cadmium ; (xx) chromium ; (xxi) bismuth ; (xxii) mercury ; (xxiii) molybdenum ; (xxiv) vanadium ; (xxv) titanium ; (xxvi) indium ; (xxvii) barium and strontium ; (xxviii) lithium and other metals. Index.

Twenty-five years ago we knew nothing about the physiological importance of any of the so-called " trace elements " except iron and iodine, and our knowledge of the biological activity of some of them is far newer than our knowledge about the function of many of the vitamins. The books on the vitamins are legion, but Dr Monier-Williams is the first to give us a comprehensive review of the trace elements.

Dr Monier-Williams defines a trace element as one which is normally present in the human body or in foods in a concentration of less than 0.005 per cent and which plays some part in the nutrition of plants or animals. He points out, however, that to the food chemist the term may equally well be applied to those elements which may accidentally gain access to foods and which have a toxicological rather than a nutritional interest.

The book is divided into 28 chapters and each deals with a different element. In the case of the biologically essential elements the part each plays in animal and plant life is first discussed. The distribution in the human body and the way in which the element is absorbed and excreted is next described, and the literature on human requirements is reviewed. The effects of a deficiency and an excess are noted, and the distribution of the element in foodstuffs is dealt with in some detail. Each chapter ends with a discussion of the chemical and physical methods available for the determination of the element in question, and a list of references to the literature on all aspects of the element is given. Copper, for example, has 253 references, zinc 110, and fluorine 126.

Elements such as lead, tin and arsenic, which are primarily of toxicological interest, are treated rather differently. The methods by which they gain access to food and drink, the toxic levels and the symptoms of poisoning are described. Methods of estimation are also given, and again each chapter is fully documented.

This book is a first-class work of reference, but it may equally be recommended as bedside literature, for it is full of entertaining statements. Who would have thought that tea is our richest source of manganese, mushrooms of silver and brazil-nuts of barium ?

The story of the trace elements is a fascinating one and it has still not all been told—indeed a new discovery has been made since the publication of Dr Monier-Williams' book, the part that cobalt plays in the anti-pernicious anaemia factor, vitamin B_{12}. More still

remains to be found out, the exact function of manganese for example, and it is to be hoped that Dr Monier-Williams will have the opportunity of revising his book from time to time. It is certain to be the standard textbook on the subject for many years to come.

E. M. Widdowson

Cancer. Volumes 1 & II

J. Maisin. Paris : Casterman, 1948. Vol. I : 248 pages. 20 × 13 cm. 540 fr. Vol. II : 306 pages. 20 × 13 cm. 600 fr.

Vol. I. Hérédité—hormones, substances cancérigènes : (i) Notions élémentaires de cancérologie ; (ii) hérédité et cancers ; (iii) hormones et cancers ; (iv) les substances cancérigènes. Bibliographie. Vol. II. Radiations—virus, environnement ; (v) radiations et cancers ; (vi) parasites, microbes, virus et cancers ; (vii) milieu, alimentation, enzymes et cancers. Bibliographie.

Doctor Maisin first began investigations in cancer research nearly thirty years ago ; he is now Professor at the University of Louvain and Director of its Institute of Cancer.

His book, *Cancer*, is a vivaciously written outline of the history, development and present position of the subject, where the reader will find the main ideas and lines of research handled with dexterity and sympathy. *Cancer* is in an attractive popular style and for those who are familiar with the usually somewhat austere publications on cancer research it gives a feeling of relief and pleasure to experience the easy fluidity of the language and the arresting dramatization of discoveries in this field. The writing would lose something in translation ; it would not be easy to find adequate expression for passages with a touch of poetry such as " . . . cette ère expérimentale qui ne sera close que par la découverte de la solution de ce vaste problème qui torture l'esprit des chercheurs." Newcomers (now to be counted by hundreds) to cancer research will find this book an attractive survey of the subject, and rather more-experienced workers will gain by a revision of those branches with which they are not perfectly at home.

Maisin in his introduction dedicates the book to " les intellectuels non spécialisés dans la question du cancer ", and consequently, with the aim of stimulating interest and not raising too many difficulties at first, he takes up a somewhat uncritical standpoint. He is inclined to give the prestige of theory to assumptions which are, at best, working hypotheses and are sometimes not much more than a product of the wishful thinking of specialists from other branches of biology who have made a forceful entry into cancer research. The author is at his best in tracing the development of the different lines of investigation and in pouring out names, dates and facts, in pleasantly assimilable form. However, he shows no hesitation in enthusiastically embracing the theories of the cytogene, mutation, the K electron region, the virus and others. This generosity towards innovators in cancer occasionally comes near to superficiality. For example, he states :

> La latence dans la genèse du cancer, qui survient parfois des mois après tout contact avec les substances cancérigènes et après que celles-ci sont éliminées de l'organisme, ne peut guère s'expliquer, si l'on admet la mutation comme base de la cancérisation, que par l'hypothèse des cytogènes de Lindegreen (voir chapitre du Virus et de l'hérédité). La substance cancérigène réaliserait la mutation du chromogène et celle-ci s'exprimerait par la modification subséquente des cytogènes qui en serait la conséquence. Nous aurons d'ailleurs l'occasion par la suite de revenir plusieurs fois encore sur cette très intéressante hypothèse. Dès maintenant, constatons qu'elle nous donne avec les altérations enzymatiques une idée du mécanisme de cancérisation applicable en commun à toutes les substances cancérigènes.

On the K electron region he says :

> Il apparaît immédiatement qu'une charge minima égale à environ 1.292 e est nécessaire pour l'apparition du pouvoir cancérigène. Au-dessus de ce seuil inférieur, le pouvoir considéré croit sensiblement en proportion de la charge de la région " K ". Il y a néanmoins un optimum de charge parce qu'une trop forte charge de la région K expose la molécule à réagir avant d'arriver à la cellule à cancériser. Le méthycholanthrène a une région K = 1.330 e. Ce genre d'étude permet de prévoir que les substances antagonistes de la cancérisation auraient une région K assez chargée et que le seuil d'inhibition serait voisin du seuil de cancérisation.
>
> Voilà une voie toute nouvelle dont le développement nous paraît plein de promesses. Il semble évident d'après ces travaux que cette région K intervient d'une façon directe ou indirecte dans la cancérisation par action sur l'une ou l'autre fonction cellulaire : catalyse, combinaison, lyse . . . Elle doit en tout cas jouer un rôle spécifique direct ou indirect dans la cancérisation, et si celle-ci est la résultante d'une mutation intervenir activement dans le déclenchement du processus.

Such a treatment can hardly be called critical ; it might be better described as acquiescence in the bolstering up of somewhat flimsy hypotheses. Maisin also shows a pathetic, albeit very human, faith in therapeutic substances, for he constantly uses terms like " anticroissance," " pouvoir d'inhibition," " substances antagonistes de la cancérisation," " des facteurs inhibitants vis-à-vis d'autres types de cancer," " antiblastique," " de fractions lipidiques qui ont des effets prophylactiques vis-à-vis du cancer du foie." Rather graver objections will be raised by the deliberate statement :

> " La vitamine A, la vitamine B 1, la vitamine PP et dans certaines conditions la B 2, sont probablement des moyens prophylactiques dont notre organisme use d'une façon plus ou moins détournée dans sa lutte contre les multiples agents cancérigènes qu'il a à combattre au cours de la vie journalière."

The irresistible need for an intellectual synthesis of the facts is of course a very attractive part of the scientific adventure, but if the data are unreliable the results of synthesis can be distressing. Maisin has been led into a booby trap by accepting the report by some American workers that lanoline inhibits carcinogenic activity. Berenblum's experiments suggested, however, that a 1 per cent (for example) solution of carcinogen dissolved in lanoline and applied to mouse skin remains a 1 per cent solution, whereas a 1 per cent benzene solution (for example) rapidly approaches a 100 per cent solution as the benzene evaporates, thus explaining the fictitious inhibition by lanoline.

Cancer will probably give the hypercritical a few shocks ; nevertheless, the book is of value because of its admirable flowing style and because of its richly comprehensive, bird's-eye view of cancer research.

I. Hieger

Nomenclature of Fungi Pathogenic to Man and Animals

Medical Mycology Committee of the Medical Research Council. London : His Majesty's Stationery Office, 1949. (Medical Research Council Memorandum No. 23.) 12 pages. 25 × 15 cm. 6d. [£0.025]

Apart from such troubles as ringworm and athlete's foot, the layman knows little of mycoses, so that English names for fungal disorders are few. The group of organisms which cause these diseases has been studied mainly from the medical standpoint. In consequence, classification has been based to a great extent on clinical characters. It so happens that for some genera this has resulted in grouping according to natural divisions, but some of the Latin names in use are invalid and the International Rules of Nomenclature have not always been properly observed. Nomenclature is a vexed question in most biological fields. The position is particularly unsatisfactory in this realm of medical and veterinary mycology, since many workers are not familiar with the appropriate mycological literature.

Of the 65 fungal species recorded in Britain, under 150 names, as human pathogens, this Memorandum lists the more important endemic species, and some which are occasionally introduced. The Actinomycetes are included, according to the classification of Waksman & Henrici. For the benefit of readers unaccustomed to mycological nomenclature, there is a short and very readable introductory account of the reasons and rules underlying the choice of names of fungi. The function of citations of authors is also explained. The names recommended for fungi and diseases are clearly distinguished from the rejected synonyms by the use of different types. Where necessary, there are brief annotations to justify the choice of particular names.

The Committee is to be congratulated on the orderly presentation of a vast amount of information in the small space of this booklet. It should help greatly to dispel the existing confusion in the field of medical mycology.

E. G. G.

PATHOLOGY & BACTERIOLOGY

The Pathology of Articular and Spinal Diseases

Douglas H. Collins. London : Edward Arnold & Co., 1949. viii + 331 pages ; 199 figures. 24 × 15 cm. £1 15s. [£1.75]

(i) General anatomy and embryology of the joints ; (ii) histology and physiology of bone, cartilage, synovial tissues and joint fluid ; (iii) a short review of bone diseases ; (iv) trauma in relation to joint disease ; (v) osteoarthritis ; (vi) gout ; (vii) bacterial arthritis—specific infections of the joints ; (viii) rheumatic fever ; (ix) rheumatoid arthritis : pathological description ; (x) rheumatoid arthritis : aetiological discussion ; (xi) disorders of the joints in diseases primarily affecting other systems ; (xii) tumours of joints ; (xiii) the spine—applied anatomy—malformations ; (xiv) the intervertebral discs ; (xv) spinal diseases : scoliosis, kyphosis, trauma, osteoporosis, Paget's disease ; (xvi) spinal diseases : tumours, infections, Pott's disease ; (xvii) spinal diseases : osteoarthritis, osteophytosis, ankylosing spondylitis. Index.

This is an excellent and much needed book and will be welcomed by both pathologists and clinicians. The ground covered is chiefly that of the common diseases of the joints, and it is curious that no previous publication has covered this familiar ground in the authoritative and readable fashion of this volume. There are many illustrations, most of them very good, and all well chosen. Each chapter is followed by a brief and well-selected list of references.

The book starts with an account of the anatomy and physiology of joints, proceeds with a brief review of bone diseases, and passes on to consideration of trauma in relation to joint disease, osteoarthritis, gout, specific infections, rheumatic fever, and of rheumatoid arthritis, and ends with interesting and useful chapters on the spine and its diseases. The author's personal post-mortem observations on four autopsies on cases of ankylosing spondylitis are of great interest, since previous descriptions have been scarce, and the previous clinical state of some of the victims doubtful.

The conclusions reached in this book are an authoritative blend of personal experience and a critical assessment of the literature. The style is simple and easy to read. It is likely to become the standard book of reference on the subject of the pathological changes which occur in the joints and in the spine.

W. S. C. Copeman

The Nature of the Bacterial Surface. A Symposium of the Society for General Microbiology, April, 1949

Edited by *A. A. Miles & N. W. Pirie.* Oxford : Blackwell Scientific Publications, 1949. vii + 179 pages ; 12 plates ; 7 figures. 22 × 14 cm. 15s. [£0.75]

(i) Introduction ; (ii) the surface structure of *Shigella shigae* as revealed by antigenic analysis ; (iii) the nature of the surface of gram-positive bacteria ; (iv) the osmotic barrier in bacteria ; (v) on the mechanism of adsorption of bacteriophages on host cells ; (vi) the status of some arguments about the bacterial surface ; (vii) the nature of bacterial surfaces ; (viii) capsule formation in the pneumococcus ; (ix) bacterial surface, flagella and motility.

At a meeting of the Society for General Microbiology held in London in April 1949 a symposium was held on the subject of "The Nature of the Bacterial Surface" at which a number of distinguished workers from other countries were invited to speak. The Proceedings have now been published in book form, and contain much of interest to workers in several fields. The subject was well chosen, since it is one on which work has converged from several widely separate directions. The electron microscope has made possible the much more detailed direct study of bacterial structure, and many beautiful photographs so obtained are reproduced. Antigenic analysis has to concern itself with the position of the substances concerned, and the obvious example of the capsular antigen is not an isolated one : others occupy a surface position. Studies of the bacterial cell wall have been made, not merely from a simple morphological standpoint, but with a view to elucidating its chemical structure and tinctorial behaviour and to explaining the mechanism by which nutrients are absorbed. The mechanism by which bacteriophage is adsorbed has also been studied. These were some of the subjects of the contributions. The last, by A. Pijper of Pretoria, South Africa, was perhaps the most controversial, and evidently gave rise to vigorous discussion. Pijper, by direct observation and microcinematography, using dark ground illumination with sunlight as the illuminant, has convinced himself that flagella are not organs of motility. This view was contested by the President of the Society, Sir Alexander Fleming, who has been studying the abnormal forms of *Proteus vulgaris* produced under the influence of penicillin, by phase contrast microscopy. Each of their contributions is freely illustrated. The usefulness of all the chapters is enhanced by an appended list of references.

L. P. Garrod

Bacteriological Technique. A Guide for Medical Laboratory Technicians

W. W. W. McEwen. London : J. & A. Churchill Ltd., 1949. viii + 293 pages ; 70 figures. 21 × 14 cm. 15s. [£0.75]

(i) Laboratory accommodation and equipment ; (ii) care of laboratory glassware and equipment ; (iii) preparing routine glassware and apparatus for sterilization ; (iv) special apparatus for collection of specimens ; (v) laboratory glassblowing ; (vi) upkeep of laboratory stock ; (vii) laboratory records of specimens ; (viii) laboratory animals ; (ix) animal post-mortem technique ; (x) sterility and sterilization ; (xi) centrifuges ; (xii) immunity and immunological technique ; (xiii) Wassermann, Kahn and similar reactions ; (xiv) general culture technique ; (xv) anaerobic culture technique ; (xvi) stock cultures ; (xvii) preparation of culture media ; (xviii) filtration of media ; (xix) culture media ; (xx) bacteriological filters ; (xxi) sections ; (xxii) routine bacteriological examination of water ; (xxiii) routine bacteriological examination of milk ; (xxiv) bacteriological examination of shell-fish ; (xxv) routine bacteriological examination of stools ; (xxvi) routine bacteriological examination of swabs ; (xxvii) routine bacteriological examination of sputa ; (xxviii) examination of hairs, etc., for ringworm ; (xxix) slide preparations for microscopical examination ; (xxx) stains, staining methods and fixatives ; (xxxi) the microscope. Index.

In Great Britain many technicians in bacteriology have not had an adequate course of systematic training in their subject and they have relied on occasional lectures or on medical textbooks to guide them in their practical work. In the introduction to this book Sir Alexander Fleming points to the need for precise and detailed instructions for the student technician whose daily tasks in the routine bacteriological laboratory are so important for reliable work. Such a book should, however, be more than a list of instructions ; in simple language it should give the reasons why certain methods are used, and it should explain the principles on which they are based. To the question whether this book serves the purpose, the answer must be a qualified yes. It would probably have gained much if an experienced bacteriologist had taken a larger part in its shaping and it suffers from the faults which the limited experience of any one technician necessarily imposes. On the other hand the author well knows the difficulties which his prospective readers will encounter, and the writing is usually clear and simple.

Such subjects as the preparation of glassware and apparatus for sterilization, the care of laboratory animals, and the preparation of culture media are well described and should prove helpful to the beginner. One would, however, have preferred to see a much more liberal use of diagrams and greater space devoted to those matters which are primarily the concern of the technician. There seems little point in publishing lists of formulae and staining techniques which are readily available elsewhere, and the chapter devoted to histological sections could well have been left out. It would be easy to enumerate omissions from the text, such as the failure to describe culture methods in examining sputum for *Myco. tuberculosis*. However, this is of less importance than the fact that the book brings together a great deal of useful information which is not easily obtained elsewhere. The chapter on the microscope is written by a physicist and, though perhaps a little difficult for the beginner, is a good account of essentials. This book is one of the first of its kind to become available in this country and as such it deserves a welcome not only from technicians but from many others who must constantly depend on the accuracy of their work.

NEUROLOGY & PSYCHIATRY

The Biology of Mental Defect

Lionel S. Penrose. London : Sidgwick and Jackson Ltd., 1949. xiv + 285 pages ; 7 plates. 22 × 14 cm. £1 1s. [£1.05]

(i) Historical background ; (ii) incidence, definition and measurement ; (iii) principles of classification ; (iv) principles of causation ; (v) methods of analysis in human genetics ; (vi) the genetics of intelligence ; (vii) rare dominant defects ; (viii) rare recessive defects ; (ix) rare sex-linked defects and the problem of sex limitation ; (x) defects of obscure origin and environmentally determined disabilities ; (xi) mental disorders ; (xii) treatment. References. Appendices. Index.

There are very few who could have written this excellent book : perhaps only Professor Penrose himself, because it is based on a complete knowledge of genetics as well as on long study of mental deficiency. For the same reason there are few who are equipped to review both aspects of the work.

The author has long known the interest and the importance of mental deficiency and sees now a need for its problems to be freshly related to those of the rest of medicine and of sociology in the light of much new knowledge. He limits his present task to a discussion of the medical and psycho-pathological problems of mental deficiency, within the framework of genetics, and succeds so well that any psychiatrist who specializes in this branch may well learn something of deficiency itself. He will certainly be roused to the need for more thorough and scrupulous case-taking than is customary, and he will discover much about the origins of the deficiencies and the possibilities and limitations of inheritance. Above all he will learn to think logically and with scientific precision before he reaches any conclusion.

A vast deal of information is contained in fewer than 300 pages, yet much of the book is most easy to read. Indeed it is probable that even the mathematical genetics could be digested by anyone who has had a moderate introduction to the mysteries of the subject.

If a first reading gives the impression that almost anything may be explained by a gene, and that nature leaves little over for the activities of nurture, it is probably due to the deliberate intention to hold up all knowledge of deficiency for assessment by the geneticist's special scales. And it is just possible, after all, that it may be true.

Again, the book seems to take as one condition all the various manifestations of mental inadequacy that have been brought together under the title of mental deficiency. There is legal and sociological convenience in treating them as a single symptom and it may be necessary to do so at the present stage of statistical study. Yet it is an over-simplification which would not appeal to those who spend their lives with mentally defective patients. If Professor Penrose does not quite mean this it is further proof that the book must be read and studied more than once. It must then be kept at hand for constant reference to its arguments and, above all, to the large number of valuable tables and appendices and references. Of these, the data in the author's Medical Research Council Report (the Colchester Survey, London, 1938), provide a great part and there is no need for his apology. He had a great opportunity and used it so well that all are in his debt.

The publishers have been helpful by making a book that is small and light and clearly printed on good paper. The only possible criticism is the unusual spelling, " chorioid," which appears on several occasions.

Noel H. M. Burke

An Outline of Psycho-Analysis

Sigmund Freud. London : Hogarth Press and Institute of Psycho-Analysis, 1949. ix + 84 pages. 22 × 14 cm. 8s. 6d. [£0.425]

Part I. The mind and its workings. (i) The psychical apparatus ; (ii) the theory of the instincts ; (iii) the development of the sexual function ; (iv) mental qualities ; (v) dream-interpretation as an illustration. Part II. The practical task. (vi) The technique of psycho-analysis ; (vii) an example of psycho-analytical work. Part III. The theoretical yield. (viii) The psychical apparatus and the external world ; (ix) the internal world. Index.

Papers on Psycho-Analysis

Ernest Jones. Fifth edition. London : Baillière, Tindall & Cox, 1948. vii + 504 pages. 22 × 14 cm. £1 11s. 6d. [£1.575]

(i) Freud's psychology ; (ii) the psychopathology of everyday life ; (iii) the theory of symbolism ; (iv) the genesis of the super-ego ; (v) psycho-analysis and the instincts ; (vi) psycho-analysis and comparative physiology ; (vii) psychology and war conditions ; (viii) love and morality ; (ix) the concept of a normal mind ; (x) Freud's theory of dreams ; (xi) the relationship between dreams and psychoneurotic symptoms ; (xii) the nature of auto-suggestion ; (xiii) the psychopathology of anxiety ; (xiv) fear, guilt and hate ; (xv) cold, disease and birth ; (xvi) jealousy ; (xvii) psycho-analysis and modern medicine ; (xviii) the unconscious mind and medical practice ; (xix) psycho-analysis and psychiatry ; (xx) the criteria of success in treatment ; (xxi) psychology and childbirth ; (xxii) some problems of adolescence ; (xxiii) the phantasy of the reversal of generations ; (xxiv) anal-erotic character traits ; (xxv) the early development of female sexuality ; (xxvi) the phallic phase ; (xxvii) early female sexuality. Glossary. Index.

Dr Ernest Jones believes that centuries must elapse before psychoanalysis comes to full fruition. Certainly half a century after its birth the status of the discipline remains ill-defined. Much of the blame for this unsatisfactory position should be accepted by psychoanalysts themselves who, like the followers of many quasi-religious movements, have refused to permit criticism except from the converted ; and for very human reasons the converted rarely criticize. It is a tribute to psychoanalysis, and perhaps also the credulousness of man, that few apostates have arisen.

Freud's discoveries of the mechanism of repression, of the formative influences of emotional attitudes during infancy, and of the unconscious determinants of human behaviour, have now been respectably incorporated in psychiatric knowledge and have animated what was, before Freud, a static collection of descriptive data. These conceptions clearly explain phenomena which have been pondered over, but never understood, ever since there were students of human nature. His pansexuality and panpsychogenesis, however, have not found the same acceptance from the common man nor from the psychiatrist, and they have been arrived at by methods that are not the tried methods of experimental science.

Because of its cost and because the therapeutic indications are restricted, the value of psychoanalysis as a treatment is limited. The few published results are not strikingly impressive ; they are perhaps equalled by simple methods of psychotherapy or even by the vis medicatrix naturae and by that healing process, the passage of time. Moreover, the dangers of psychoanalysis are real and the greatest of these, especially when lay therapists are in control, is the risk of delay in applying physical methods to the treatment of a schizophrenic psychosis. It is as a technique of exploration of the roots of psychogenic illness that the place of psychoanalysis is more assured.

In America the acquisition of a psychoanalytic orientation has become almost a necessity of life for psychiatrists ; in Europe no such widespread recognition of psychoanalysis has been afforded, but orthodox psychoanalysis has been less eroded by short-cut techniques. In both continents there is a great shortage of facilities for training in psychoanalysis, so that works such as those noticed here are indispensable to every psychiatrist and perhaps to every educated person.

Freud's *Outline* was his definitive but unfinished account of his doctrines and it was first published, in German, in 1940. The translation is excellent and, like all Freud's writings, the exposition is lucid, persuasive and free from non-essentials. There is here nothing new, but as Freud all his life adapted his views so that they might accord with new knowledge, his final thoughts have special value and the book will be a psychoanalytic classic.

Dr Ernest Jones' *Papers* were published first in 1912 and the present edition is likely to be the last. It omits 14 papers that appeared in the 4th edition, and includes 9 more recent essays. All the 27 papers, which vary much in length, have been previously published elsewhere. The topics range from " The psychopathology of everyday life " to " The theory of symbolism ", and the latter, first written in 1916, is generally recognized as a specially valuable contribution to psychoanalytic theory. Freud has not always been fortunate in his interpreters but in Dr Jones he has always had a powerful disciple. Like the *Outline*, the *Papers* are addressed to both lay and medical audiences ; the latter will be particularly interested in the short essays on the relations of psychoanalysis to medicine and to psychiatry.

Hunter Gillies

Human Personality and its Minor Disorders

William Harrowes. Edinburgh : E. & S. Livingstone Ltd., 1949. vii + 260 pages ; 22 × 14 cm. 15s. [£0.75]

(i) General principles of adaptation ; (ii) psychobiology and historical background ; (iii) introduction to personality study ; (iv) special analysis of the

psychobiological assets; (v) the topical processes and assets; (vi) the topical processes and assets (*continued*); (vii) range and fluctuation of fitness with regard to the ratio of work, play, rest, and sleep; (viii) social relations and the relative role of self-dependence and social dependence; (ix) sex development and patterns; (x) synthesis and balance of the personality; (xi) difficulties and handicaps; (xii) reaction to disappointments, etc.; (xiii) origins of assets, liabilities, and determining tendencies; (xiv) minor personality disorders; (xv) anxiety states; (xvi) obsessive-compulsive-ruminative tension states; (xvii) hypochondria; (xviii) neurasthenia; (xix) hysteria; (xx) treatment. Bibliography. Index.

To have written a book on personality which is both readable and well balanced is no small achievement. Dr Harrowes has formulated a concept of human personality which is based on the direct observation of normal persons, who are described in terms of "non-dogmatic objective common sense". In this he has been guided very largely by the views of Adolf Meyer, of whom he was a pupil and to whom he acknowledges his debt. The approach is practical rather than theoretical and the points are illustrated by descriptions of actual patients seen at the psychiatric clinic and by examples taken from a wide range of general literature.

The first part of the book is taken up mainly with an analysis of the psychobiological dimensions of the normal individual, in which the general principles of adaptation to the environment are discussed. The later chapters deal with the commoner forms of personality disorder, concluding with a brief chapter of practical notes on treatment. Here emphasis is laid on the need to encourage the patient towards the satisfaction of actual achievement—"the final and only real test of the effective organisation of human personality". Several of the chapters are furnished with lists of questions, which may be helpful to the student.

The presentation of the material is lively and informal in style: but yet Dr Harrowes is never superficial, for he is clearly drawing from an uncommonly wide range of experience. His conclusions are based wherever possible on sound physiological data and he frequently goes back to first principles in his analysis of cause and effect. He is careful in his use of words, many of which he defines in relation to their roots in the Sanskrit, and he has generally managed to avoid the difficult vocabulary of the psychoanalytical schools.

This book will clearly be of value to the student and to many others who seek a readable and informative account of personality expressed in terms of objective common sense.

Derek Richter

Mr. Carlyle, My Patient. A Psychosomatic Biography

James L. Halliday. London: William Heinemann Medical Books Ltd., 1949. xiii + 226 pages. 22 × 14 cm. 15s. [£0.75]

Introduction to the patient. Part I: Early emotional development. (i) Infancy—experience of the mother; (ii) infancy—experience of the father; (iii) school-days; (iv) college days; (v) teaching; (vi) relations to men—Edward; (vii) the curriculum of dyspepsia begins; (viii) relations to women—Margaret; (ix) no object—no rest; (x) Miss Welsh; (xi) Mr. Carlyle meets Miss Welsh; (xii) the year that followed; (xiii) the fire baptism, and its sequel; (xiv) unsettled years (1822–1824). First interlude. Part II: The annals of later emotional development. (xv) Getting married (1825–1826); (xvi) Comely Bank (1826–1828); (xvii) Craigenputtock and Sartor (1828–1831); (xviii) death of the father (1832); (xix) Craigenputtock resumed (1832–1834); (xx) London and "the French Revolution" (1834–1837); (xxi) the hero is delineated (1838–1842); (xxii) the hero and the lady (1843–1847); (xxiii) the hero is rampant (1848–1850); (xxiv) the hero is "imprisoned" (1850–1853); (xxv) death of the mother; (xxvi) the sound-proof room (1854–1866); (xxvii) death of Jane; (xxviii) the dance of dying dreams (1866–1881). Second interlude. Part III: The patient's mind and ideas. (xxix) His sociology; (xxx) his theology; (xxxi) his politics; (xxxii) his ideology. Good-bye to the patient. Supplement and appendix: Carlyle as literary artist; the path of life; sources; acknowledgments; apology.

For some time past, psychoanalysts have sought to win their spurs in the literary field by producing psychoanalytical biographies of some one or other of the great figures in history or fiction. Freud himself was responsible for setting this fashion; although it should be noted that, whereas Freud's biographical studies usually ended in some discovery of significance, the essays produced by most of his followers have rarely done more than recapitulate standard analytical theory as illustrated by the life of their particular subject.

It would now appear that psychosomatic specialists, those camp-followers of clinical psychology who post themselves on the frontiers of body and mind in order to study "functional disorders", have been fired by similar ambitions. Having no psychopathology of their own to offer, they usually fall back on an eclectic compost of theories derived as a rule from Freud, Jung, Adler or anyone else they fancy.

Dr Halliday's book is a case in point. Apparently familiar with the outlines of Freudian theory, but obviously influenced to a marked degree by Jungian ideologies, he has produced a book which purports to be a psychosomatic biography. Adopting the journalistic device of pretending that Carlyle had visited his consulting-room, Dr Halliday comes to the conclusion that the Sage of Chelsea suffered from an organ-neurosis of the stomach due to emotional stress, which in turn was due to unconscious homosexual longing and an early hunger for mother-love. Carlyle, the author informs us, was an "anal" character of a psychopathic type, with definite paranoid traits, sadistic and masochistic tendencies and schizoid features. He was also, it appears, hypochondriacal, somewhat cyclothymic and just avoided a psychotic breakdown. "Psychosocially" regarded, Carlyle belonged, we are told, to a "sick family group", which is held to account for his sociological, theological and political views.

The truth is that the author has fallen heavily between two schools. Whatever may have been the psychiatric diagnosis of Carlyle's condition, Dr Halliday's book does nothing to illumine the subject; and, despite its title, says little about the psychosomatic aspects of the case. Copious and sometimes tendentiously chosen excerpts from Carlyle's works (*Sartor resartus* is sometimes treated as factual biographical material, sometimes as a substitute for dream or phantasy) are interspersed with analytical glosses which are little more than summaries of infantile development such as might appear in any elementary textbook of eclectic theory. Only at the very end of the book, by the way, is the general reader informed that the "psychological processes associated with Carlyle's development were largely *unconscious*".

With all this there is not, as far as can be seen, the slightest attempt to account for anything that was not obviously accounted for before. It is no explanation of Carlylean hyperbole to maintain that this is an indication of an underlying psychotic tendency. As for the Carlylean genius, this is precisely what Dr Halliday is unable to account for, a fact which deprives his book of any visible *raison d'être.*

Edward Glover

Die Einteilung des Nervensystems nach seinen Leistungen

L. R. Müller. Second edition. Stuttgart: Georg Thieme, 1950. 74 pages; 21 figures. 24 × 17 cm. 8.70 Mk.

(i) Einteilung des Nervensystems nach seiner äussern Form; (ii) Nomengebung der funktionellen Einteilung des Nervensystems; (iii) Umweltnervensystem (systema pro mundo); (iv) Nervensystem für unwillkürliche Muskelspannung und für Korperhaltung (systema nervorum myotonicum et myostaticum); (v) Lebensnervensystem (systema nervorum vitale); (vi) Beziehungen des Umweltnervensystems zum Lebensnervensystem; (vii) Einteilung des Nervensystems nach seinen seelischen Leistungen; (viii) progressive Zerebration der seelischen Vorgänge; (ix) Beeinflussung der seelischen Vorgänge durch Stoffzufuhr oder Stoffmangel des Blutes; (x) Psychoanalyse; (xi) seelische Veranlagung; (xii) Beziehungen der Seele zum Nervensystem.

This book is an enlarged edition of the 1933 publication, in which L. R. Müller introduced a new classification of the nervous system into three parts, according to their functions. Firstly is the part concerned with the surrounding world, the *systema nervorum pro mundo*. It consists of the sense organs with their nerves and central representations; the thalamus and the whole cerebral cortex are included in this system. Secondly is the part concerned with automatic movements and muscle tone, the *systema nervorum myostaticum*. The extrapyramidal system with parts of the thalamus and the cerebellum are the main parts of this system. The third part is concerned with visceral functions, the *systema nervorum vitale*. The autonomic nervous system, its central representations, the sensory nerves from the viscera, the hypothalamus, and the centres in the medulla and spinal cord make up this system. An attempt is made to discuss with this classification the mind, emotions, memory, will and consciousness. It is not surprising that Müller's classification has not been accepted in the past sixteen years, and it is unlikely that it will be so in the future. It provides no help for clinical, physiological or anatomical research and is not a fruitful guide for the understanding of the nervous system. The book certainly contains a number of interesting facts and observations, but it takes no account of the present trends of research. One feels as if one were reading a book from the past—but that has a certain attraction.

W. Feldberg

SOCIAL MEDICINE

Tuberculosis: a Global Study in Social Pathology

John B. McDougall. Edinburgh: E. & S. Livingstone Ltd., 1949. viii + 455 pages; 29 figures. 25 × 18 cm. £1 12s. 6d. [£1.625]

Part I. Introduction. Mortality rates and other data concerning tuberculosis in different countries of the world. Part II. Some general considerations influencing morbidity and mortality rates from tuberculosis—a summary of prevailing views. Part III. Investigating the tuberculosis problem in a community—with commentaries. Part IV. Evaluating the problem. General index. Geographical index. Index of authors and sources quoted.

It was not so very long ago that we were content to study the epidemiological problems of tuberculosis by collecting information in the confined area of a few streets. These unambitious surveys led to observations in wider fields, and the statistics of cities and counties were compared. Then mass observation was established, and the possibility of the rapid examination of thousands of persons by miniature radiography made any statistics involving less than a thousand persons appear inadequate. The book under review has followed the general tendency of examining data derived from the study of very large population groups. In fact it is, as its title suggests, a most ambitious project amounting to nothing less than a study of tuberculosis in well over one hundred different countries distributed throughout the five continents. The object of the work is to present information on infection, morbidity and mortality from tuberculosis, and also to analyze the factors usually considered to have a bearing on the extent and severity of the problem in large groups of population. It is inevitable that criticisms can be made in so comprehensive a study, but on the whole it is remarkable how successfully the author has achieved the object of the task he set himself.

The book is divided into four parts (see details at the head of this review). Following the mortality and morbidity figures, the author gives, in the majority of cases, comments on the figures, although there is a tendency to quote too many authorities in these commentaries; this tendency rather overshadows and may even suppress the valuable observations of the author himself.

Two features are stressed in the general observations on statistics relating to incidence and mortality rates of the 31 countries in which it is possible to be reasonably certain of the accuracy of the figures. These are that in all countries there has been a very considerable fall in the tuberculosis mortality rates during the last fifty years, and that, although the war periods caused a rise in all devastated countries, the rates have, in the majority of instances, fallen almost to pre-war levels within three or four years after the cessation of hostilities. The reasons for the decline in mortality for each country are discussed in detail.

In the part devoted to general considerations influencing mortality and morbidity rates, the author is on less certain ground, but tackles these debatable problems with characteristic lucidity. There is a tendency to confuse "native" and "acquired" resistance, and there are a number of generalizations that will not be accepted by many readers. For instance, it is doubtful whether proof can be found to support the statement that ". . . the school age group is further fortified by possessing a natural resistance which is probably greater than at any other period of life . . ." (page 165), neither will all clinicians agree that caseation is more frequent and cavity formation more rapid at the age of puberty than in adult life (cf. page 166). Even more contentious is the statement that "It is established, in fact, by careful follow-up work, that the more intense the allergy-potential the greater the risk of developing tuberculosis" (page 269). It would, however, be unfair to analyze in this manner every paragraph in a work that sets out to be a global survey. The author has no hesitation about the great importance of environment and standard of living as factors determining the likelihood of suffering from active tuberculosis in any particular individual.

There is an interesting section on the study of tuberculosis mortality in successive generations, and a number of charts indicate the close relationship between the incidence of infection and tuberculous disease in infancy and childhood, and the subsequent course of tuberculosis in adult life.

Throughout the book the author makes statements that are based on his wide experience, and many of them could be hung up with advantage as texts in chest clinics in all parts of the world. One which refers to diagnosis is particularly significant in these days of mass radiography and the tendency to come to rapid conclusions—sometimes on insufficient clinical evidence. It reads, ". . . it is unfair to the patient, and scientifically unsound, to give a verdict of 'tuberculosis' on any *x*-ray film which leaves the least margin of doubt as to its correct interpretation" (page 288). Another statement which has a message at the present time, particularly in Great Britain, is, "Tuberculosis is a preventable disease, if adequate public health and socio-economic measures are taken to prevent it" (page 440).

There is no doubt that McDougall has produced a great book that will be of value to all who study tuberculosis and are engaged in combating the disease. The book is accurately indexed and well produced. It achieves its object, and helps to clarify our understanding of this world-wide problem.

Frederick Heaf

Report of the Committee on Nutrition

British Medical Association, Committee on Nutrition. London: British Medical Association, 1950. 106 pages; 3 figures. 24 × 15 cm. 7s. 6d. [£0.375]

(i) Introduction and summary of main conclusions; (ii) nutritional requirements; (iii) food consumption in the United Kingdom; (iv) clinical assessment of the nation's health in terms of nutrition; (v) psychological and practical aspects of nutrition; (vi) recommendations.

This is the report of a Committee which consisted, by its own definition, "of men and women deeply interested in the subject, who knew the language of science, and who were themselves engaged in certain of its aspects", and which was asked to make a survey that would provide answers, to "questions that frequently arise". The questions and answers are not defined and must be inferred from the general argument. The chosen field of enquiry is covered in four sections: nutritional requirements, food consumption in the United Kingdom, clinical assessment of the nation's health in terms of nutrition, and psychological and practical aspects of nutrition. The last verges on the trivial and platitudinous.

The treatment of requirements varies from one part to another. A new approach to the question of energy requirements is begun by the definition, in terms of height and weight, of a reference (or average) man and woman who are recognizable as belonging to the rank and file of the population of Great Britain and whose primary needs are estimated in accordance with generally acceptable principles. Discussing the assessment of requirements for work, the Committee was clearly aware of the danger of dividing work into only three classes, such as light, heavy, and very heavy, but did not explain that the danger arises from the tendency to place far too many workers in the higher classes and so over-estimate needs. The proposed replacement of three by six grades, defined in terms of energy expenditure per hour of work, without any guidance on the placing of occupations within these grades, goes no further towards making possible a detailed estimate of the total energy needs of the population. The Committee accepts the convention that the reference man and woman are moderately active, and this, with their definition of the reference man and woman, gives a procedure closely similar to that adopted in the *Report of the Committee on Calorie Requirements* (FAO Nutritional Studies No. 5, Washington, 1950) just issued by the Food and Agriculture Organization.

On the subject of fat and protein in the diet, the Committee takes a straightforward and practical attitude; on the assumption that energy needs are known, the proportions to be supplied by fat and protein are defined. This allows the consumption of fat and carbohydrate to be varied in accordance with habit and preference and avoids the conflict between theory and practice which arises in respect of the protein allowances of the National Research Council of the United States of America (NRC). The Committee is a little apologetic about the simplicity of this method of estimating protein requirements, but common sense is often a better practical guide than theory.

The requirements of calcium and vitamins, except for vitamin C, are the same as, or not greatly different from, the allowances proposed by the NRC in 1941 and 1945. Needs for vitamin A and the B group have been adjusted and for vitamin C assessed at lower levels in the light of recent research in the United Kingdom.

The average requirements per head of the population are com-

puted on the basis of the NRC allowances, and the estimates approved by the Committee. The results are substantially different only for vitamin C; the estimated need for vitamin A is a little higher, and that for B vitamins somewhat lower, on the new proposals. In Great Britain the 1941 allowances of the NRC were used by the Ministry of Food as criteria of the adequacy of the national diet throughout the war. The 1945 revision made only minor changes.

The Committee next reviewed information supplied by the Ministry of Food on the retail level of food supplies during and since the war, and on the family food surveys made by the Ministry of Food and other investigators. From this survey it appears that food was in short supply in 1940 and 1941 and that not only total supply but the equality of distribution, in relation to needs, improved from then to 1945. The Committee summarizes the changes in food supplies that occurred and politely disposes of the mis-statements, especially regarding foods of animal origin, which were so common in the press when the Committee began its labours. Its doubts about the adequacy of energy supplies, assessed in relation to the NRC (1941) reference standard used by the Ministry of Food, might have been less persistent if the Committee itself had been able to resolve the problem of the allocation of the adult population to correct work categories. Appendix C and fig. 1 of this section will be of special interest to those who have not previously seen an analysis of the data concerning the consumption of food during the Second World War.

The most important inference to be drawn from the discussion of the food supply survey is the implicit endorsement by the Committee of the policy of sharing in accordance with needs. If the strength of that approval is, on one hand, weakened by complaints of deterioration in variety and palatability of the diet, it is perhaps reinforced by the complaints of scantiness of data. It is, in any case, a welcome lead to members of the community who have themselves no vision of the importance of diet in social medicine.

The presentation of clinical data on the health of the people is, on the whole, fair and clear, and the graphs of death-rates are impressive additions. The discussion is cautious and it could easily be argued that the evidence, taken with the deterioration in housing and opportunities for institutional treatment of disease during the war, which is stressed only in relation to tuberculosis in children, suggests a much closer correlation of improved health with better food than with medical treatment. The comparison made is with pre-war trends and, after 1941, many indexes of health were better than the trend instead of worse, as might have been expected from earlier war experience. Whatever the reasons for the improvement, no one can question the magnitude of the achievement, and the cautious approval of a careful committee is worth more than any amount of praise from uncritical enthusiasts. "The health of the population as a whole . . . has been well maintained."

The recommendations lay fresh emphasis on the importance of a planned policy for adequate food and distribution according to needs. Much more basic information on needs, especially in relation to industrial work, is required. This is highly technical research, not easy to get going. Perhaps the Committee, or the British Medical Association, has in mind ways in which it could give help with this and with the problem of education in nutrition, which certainly should be of immediate concern to them.

I. Leitch

Examination of Waters and Water Supplies

Originally written by *J. C. Thresh, J. F. Beal & E. V. Suckling.* Sixth edition revised by Edwin Windle Taylor. London: J. & A. Churchill Ltd., 1949. xii + 819 pages; 24 plates; 28 figures. 25 × 16 cm. £3 10s. [£3.5]

Part I. Geological considerations and suitability of water for public supply purposes. Part II. Inspection of waterworks and sources of supply. Part III. The scope of physical, biological and chemical examinations. Part IV. Analytical processes and methods of examination. Part V. Analytical characters of waters in relation to their geological origin. Part VI. The bacteriological examination of water. Part VII. Results and standards in the examination of samples of water. Part VIII. Water supplies and disease. Part IX. The purification and treatment of water. Plates. Appendix. Index to analyses. Index.

A book which has been revised five times since its 1st edition in 1904 is unlikely to contain many errors. The present revised edition has been brought completely up to date but the format of the original has been maintained.

The whole book is of such a high standard of accuracy that it is to be regretted that the author does not make clear the meaning of free chlorine in the statement on page 213: "Free chlorine in the form of hypochlorite or 'chloramine' is not found in natural waters . . ." Also, it is the free chlorine and not the residual chlorine which should be maintained between 0.2 and 0.5 parts per million in swimming-bath waters (see page 712).

The analytical and bacteriological methods comprise some of the most recent advances, as instanced by the use of brilliant green broth at 44°C. to establish the presence of faecal coli. It would have been a further advantage if, where a variety of methods has been outlined for a particular determination, Dr Taylor had indicated his choice of method. The expression of results as parts per million instead of parts per 100,000 is particularly welcome.

This good book could be better: more diagrams to illustrate several sections would be welcome. In the chapter on swimming-bath water, although there are six full tables, there is not a single illustration. Again, the index, although lengthy, does not give help to the reader in looking for guidance on the important subject of the examination of waterworks employees.

In recording congratulations to the author, one should also include his wife, for he, as he himself acknowledges, like many another author has received great help in the arduous task of compiling so large a book. Dr Windle Taylor has devoted special attention to biological considerations in this edition and the plates drawn by his wife are excellent. Dr Taylor also has the advantage that he can call upon the unique and enormous experience of the Metropolitan Water Board.

The publishers and printers deserve congratulations for a well-produced volume, in which the reviewer has not found one typographical error. Here is a veritable bible for water and civil engineers, medical officers of health, analysts and chemists; here is a standard work, excellently revised, a full and indispensable guide to a pure and safe water supply.

J. L. Burn

HISTORY & BIBLIOGRAPHY

A Short History of Physiology

Kenneth J. Franklin. Second edition. London: Staples Press, 1949. 147 pages; 16 figures. 22 × 14 cm. 10s. 6d. [£0.525]

(i) The rise of physiology in the ancient world; (ii) Ibn an-Nafis (c. 1210–1288); (iii) Leonardo da Vinci (1452–1519); (iv) Jean Fernel (1497–1558); (v) Andreas Vesalius (1514–1564); (vi) publications by Servetus (1553), Columbus (1559), Botallus (1564), and Caesalpinus (1571 and later); (vii) the valves of veins; (viii) William Harvey (1578–1657); (ix) the seventeenth century; (x) the eighteenth century; (xi) the nineteenth century. Epilogue. Index.

Some knowledge of the historical background is indispensable to every student of physiology. Sir Michael Foster made this clear half a century ago in his *Lectures on the history of physiology* (University Press, Cambridge, 1901), but since that date there have been relatively few contributions to the subject. Thus the time is opportune for the appearance of Professor Franklin's compact little work, the second edition of a still smaller book which he published in 1933. Within the compass of 140 pages he has skilfully presented a complete compendium of the history of physiology. The fatherhood of physiology is attributed by some to Erasistratus, by others to Galen. Both were of the Alexandrian School, with four centuries between them. Certainly Galen was a great experimentalist and it was unfortunate that the continuance of his work was obliged to await the appearance of Vesalius. Of course Harvey was the central figure of experimental physiology, and the events which led to his great discovery are clearly set forth by Professor Franklin. A chapter on Jean Fernel, who was so highly praised by Sir Charles Sherrington, is followed by an account of Harvey's precursors—Servetus, Columbus, Caesalpinus, and the less famous Botallus, each of whom came very near to the discovery. It was Harvey's teacher, Fabricius, who supplied the clue. *De venarum ostiolis* (L. Pasguati, Padua) was the title of Fabricius' work which set Harvey thinking. After Harvey had completed his demonstration of the circulation, much remained to be done. The opportune discovery of the microscope and the foundation of the Royal Society led the way to further advances. Harvey's work was crowned by Malpighi, who revealed the capillaries, and by Boyle, Hooke and Lower, who sought to prove just why the blood circulated. The mechanical view of life gained adherents, and one of its pioneers was René Descartes, whose work suggested that neurophysiology had much in common with philosophy, a view which has gained acceptance in our own time.

The eighteenth century brought forth such giants as Albrecht Haller, and our own John Hunter, and from this stage until the end of the book every page is crowded with names and dates. Although this is unavoidable in a short work, it may be rather perplexing to the student. Perhaps a few of those names might have been omitted, or at least relegated to foot-notes, in order to leave room for a fuller account of the work of Claude Bernard. True, not a word is wasted, but close reading is demanded. The writer might have expanded his work by entering the present century, but perhaps he did wisely to round off his short history by a reference to Emil Fischer's "enzymes" of the 1890's. It is to be hoped that in a future edition, which is sure to be demanded, Professor Franklin will not only cast his net wider but will elaborate some of those charming glimpses of the pioneers of physiology which he has already set forth in such a brief compass. But even as it stands no physiologist and no student of physiology can afford to neglect this excellent historical synopsis.

Douglas Guthrie

Tuberculosis in History, from the 17th Century to our Times

S. Lyle Cummins. London: Baillière, Tindall & Cox, 1949. xiv + 205 pages; 12 plates. 22 × 15 cm. £1 1s. [£1.05]

Part I. The British School. Part II. The early continental phthisiologists. Part III. Two remarkable figures in the history of tuberculosis. Index.

Stevenson Lyle Cummins, former David Davies Professor of Tuberculosis in the Welsh National School of Medicine, who died on 26 May 1949, was an internationally recognized authority on tuberculosis who, through his modesty, charm, and personal integrity, had endeared himself to all who knew him. Retiring to Thaxted, in Essex, in 1942, he spent much of his time delving into the history of tuberculosis, and in 1945 and 1946 he read before the Section of the History of Medicine of the Royal Society of Medicine a series of papers on pioneers in tuberculosis. These he expanded and published just before his death under the title, *Tuberculosis in history*.

This book was eagerly awaited not only by the author's personal friends but by many medical historians and specialists in tuberculosis, who were hoping for an authoritative and pleasantly written work on the history of the disease by one so eminently fitted for this task by reason of his expert knowledge and his wide culture. Having had his appetite whetted by the book's attractive appearance and its wealth of artistic plates, the reader will sooner or later find himself irritated by the carelessness of the compilation, the numerous misprints, and the useless, amateurish index. Cohnheim, for example, appears as "Conheim" in several places, including the index; Lawrason Brown as "Lawrensen Brown"; Sigerist as "Sigerst"; Lettsom as "Lettsome"; Creighton as "Crighton". On page 183 Sir William Watson Cheyne is described as "M.B., F.R.C.S."; and on page 200 as "M.D., F.R.C.P.". Many of the German quotations are inaccurate.

Having overcome his prejudices, the reader will find much to interest him in this book, which consists of three Parts (see details at the head of this review). The first deals with such men as Christopher Bennet, Thomas Willis, Richard Morton, James Carson, George Bodington, and William Budd. The second Part gives biographical sketches of Auenbrugger, Corvisart, Bayle, Laënnec, Villemin, and the third is devoted to Edward Livingston Trudeau and Robert Koch. The chapter on James Carson (1772–1843) is particularly worth studying, dealing as it does with a neglected pioneer in artificial-pneumothorax therapy.

W. R. Bett

Happy Toil: Fifty-Five Years of Tropical Medicine

Leonard Rogers. London: Frederick Muller Ltd., 1950. xvi + 271 pages; 8 plates; 20 figures. 22 × 14 cm. 18s. [£0.9]

(i) Early years and education, 1868–1892; (ii) military duty in India, 1893–1896; (iii) kala-azar investigation in Assam, 1896–1897; (iv) reversion to military duty—rinderpest research; (v) general account of life in Calcutta, 1900–1920; (vi) work in the Sanitary Department; (vii) amoebic dysentery and liver abscess, 1900–1912; (viii) snake venoms, 1901–1903; (ix) differentiation of tropical fevers; (x) the cure of cholera, 1906–1917; (xi) foundation of Calcutta School of Tropical Medicine and Hygiene; (xii) interruptions of research; (xiii) epidemiology and treatment of leprosy and tuberculosis; (xiv) epidemiology of diseases in India: forecasting epidemics; (xv) later London life. Appendix I. Appendix II. Index.

The reader of this work is held spell-bound by the record of its author's industry and the sum of his achievements. His activities encompassed the diseases he studied in their widest aspects: epidemiology, natural history, cause, pathology and treatment. The solution of a concrete problem led him on to wider issues. This is well illustrated by his work on leprosy, perhaps his greatest achievement. He first identified himself with treatment, and, satisfying himself that cases are amenable to successful treatment in their early stages, he postulated that if early cases were brought to light and treated, the incidence would be reduced. Confronted with an administrative system which made pariahs of lepers, he realized that early cases, in their efforts to maintain a place in society, were being driven out of the orbit of the services designed to help them. There followed the abolition of compulsory segregation and the foundation of the British Empire Leprosy Relief Association.

Other noteworthy results of Sir Leonard Rogers' impact on tropical medicine were seen in the differentiation of the dysenteries, the pathology and treatment of amoebiasis, the treatment of cholera, the differentiation of fevers occurring in the tropics, the culture of *Leishmania donovani* and the demonstration that this parasite is a flagellate. However, he encountered failure as well as success. An attempt to extend the chemotherapeutic principles he had applied in leprosy to the treatment of tuberculosis was a cause which he loved and lost, but the disappointment incidental thereto left him undaunted. He carried his zest for enquiry and research on furlough, and after his retirement from India in 1920 his mature wisdom continued to be productive. During furlough in England

in 1903 he investigated the action of snake venoms and carried out experiments which were the basis of the successful local treatment of snake bite. Among his many activities since retirement to England have been studies of the epidemiology of various diseases occurring in India in their relation to meteorological conditions, and the formulation of bases on which epidemics may be forecast.

The Calcutta School of Tropical Medicine and Hygiene which, with the associated Hospital for Tropical Diseases, he was largely instrumental in founding, bear witness to the integration of thought and action which ran through his work. His identification with the functions of these institutions is commemorated by a marble bust in the first named, raised by subscriptions from the medical profession in India as a tribute to his services to tropical medicine.

J. Bennet

A Biography of Sir Benjamin Ward Richardson

Arthur Salusbury MacNalty. London: Harvey & Blythe Ltd., 1950. vii + 92 pages; 1 illustration. 22 × 14 cm. 7s. 6d. [£0.375]

(i) The dedication to medicine; (ii) the medical student; (iii) the general practitioner; (iv) the physician; (v) work on tuberculosis: marriage; (vi) researches in physiology and pathology; (vii) researches into anaesthetics; (viii) the prevention of disease; (ix) the campaign against alcohol; (x) studies in general literature; (xi) last days and death. Bibliography. Correspondence. Index.

Sir Benjamin Ward Richardson was a many-sided personality, sometimes paradoxical and often original. As a young practitioner he had a reputation for making whisky punch: subsequently, he became one of the great temperance advocates. A research worker and a teacher of physiology, he opposed experimentation on live animals for teaching purposes. He wrote a book on health in relation to occupation and ways of life, and his rich humanity led him to devise methods of painless killing of animals. He was a president of the Tricycle Union and the Union of Cyclists. Like a number of other distinguished medical men of the 19th century, he was interested in general literature. He wrote a "three-decker" novel, *The son of a star: a romance of the second century* (1888); several poems; and three plays (which admittedly were never performed, and were published in the *Social Science Review*, an unlikely place except that Richardson was editor). More important were his biographies, and, of course, the *Asclepiad*, which he edited.

After serving an apprenticeship with a country doctor in Leicestershire, Richardson studied medicine at Anderson's College, Glasgow. Eventually, he came south to be assistant to Dr Robert Willis in Mortlake, near London. There he worked in general practice and also did private experiments. He won a prize for an essay "Diseases of the foetus in utero", and was horrified when a publisher turned the subject down on the grounds that practitioners would not be interested in learning about diseases which took place before birth; however, on leaving the publisher, Richardson met the editor of the *Medical Times and Gazette*, and this led to his introduction to medical journalism. At the age of 26 Richardson set up practice in London, and if he never reached the front rank of London consultants he rapidly gained a wide reputation. He became a lecturer, and later dean, at the St George's Medical School, near St George's Hospital. As an expert witness, he was called at the trials for murder of William Palmer, M.R.C.S., the Rugeley poisoner, and of Thomas Smethurst, M.D.

Of his temperance views, Richardson tells (*Total abstinence, a course of addresses*, Macmillan, London, 1878) that about 1869 he first began to abstain, at intervals, "for experimental purposes." Once more it was the experimental method which led him to a certain conclusion: he became a total abstainer. His Cantor Lectures to the Royal Society of Arts not only dealt with physiological and chemical aspects of the subject, but included interesting glimpses into the history of alcoholic drink—how hops, for instance, began to be introduced into beer only in the 19th century; an order in Henry VI's reign prohibited the practice on the ground that it spoiled the beer. To appreciate how great a change Richardson helped to effect by his teaching, it is necessary to consider not so much temperance societies as the use of alcohol as a therapeutic agent. Nowadays alcoholic drinks are not often prescribed; as a measure of some current opinion on their use in illness it may be pointed out that such prescriptions are not covered by the National Health Service. Yet when Richardson began his campaign "a doctor who did not prescribe alcohol freely was not only avoided by patients but was regarded as heterodox and more than eccentric by his professional brethren." That this has all changed is due in measure to Richardson, who suffered for his "extreme" views.

Richardson held strong opinions on vivisection and tobacco smoking. Of vivisection he held that experiments should be performed only for a definite object, and painlessly. In a characteristic passage in his book, *Biological experimentation, its functions and limits*, published in London in 1896, he says of his own use of live demonstrations in the teaching of physiology: "To be plain, I soon gave up experiments in my class, not from any sentiment, but because I got on better without them". Of tobacco smoking he wrote (*For and against tobacco*, Churchill, London, 1865): "The luxury is not directly fatal to life, but its use conveys to the mind of the man who looks upon it calmly, the unmistakable idea of physical degradation." He thought that it was because most women did not smoke that the continued integrity of the race was preserved.

One of Richardson's active interests was the prevention of disease, and he was the first Chairman of the Royal Sanitary Institute. Some of his public health schemes were idealistic; others have since been adopted. He was keenly concerned with the integration of mental and physical well-being, and considered that medical men are the happiest members of the community (*Diseases of modern life*, Macmillan, London, 1876).

Richardson was knighted in 1893 "for services to humanity". It is characteristic of the man who was "never tired" that at the age of 65 he tried to take up a new career by standing as a candidate for Parliament. Eventually the end came in 1896; and because Richardson had been an advocate of cremation, his body was cremated at Brookwood, in Surrey. Sir Arthur MacNalty sums him up as "... a physician, a man of science and letters, a philanthropist, a mystic and an ardent social reformer." Sir Arthur is to be congratulated on a biography that is concise and full, and which is adequately documented and indexed.

Laurence Dopson

English Index to Soviet Medical Periodicals Available in London Libraries, Together with a Location List of the Periodicals Indexed. Volume I, 1945-1947

Edited on behalf of the Medical Committee of the Society for Cultural Relations with the U.S.S.R. by *Donovan T. Richnell.* London: H. K. Lewis & Co. Ltd., 1950. xi + 93 pages. 28 × 21 cm. £1

An important omission in medical bibliography—especially noticeable since the termination of the last war—has been the failure to provide an adequate English index of Soviet medical literature. As the result of this, workers in English-speaking countries have been gradually losing touch with medical progress in the USSR. However, this state of affairs is not entirely the fault of the bibliographical services, but is to some extent due to causes beyond their control. One of these is language difficulties, especially since Soviet journals have given up the useful practice of supplying, in some foreign language, translations of the titles and summaries of the papers. The other is the increasing difficulty experienced by scientific institutes and abstracting journals in obtaining the necessary Russian periodicals.

This index was compiled by Mr Richnell on behalf of the Medical Committee of the Society for Cultural Relations with the U.S.S.R. with the object of filling the gap in the indexing of Russian medical literature. The present volume contains references to papers published in the years 1945–1947, while those appearing subsequently will be included in future volumes.

The arrangement of the material follows that adopted in the *Quarterly Cumulative Index Medicus*, and the present publication can be regarded as its supplement devoted to Russian works. References to papers are arranged in alphabetical order, and comprise, on the one hand, a subject heading which is the main entry for each item, and, on the other hand, authors' names, both entries containing the name of the journal, with year, number and page. The transliteration of Russian names does not follow any particular system, but conforms to English phonetics.

In the introductory pages is a list of journals indexed, with English translations of their names (Part II). There is also a list of the parts indexed (Part III), and finally a list of libraries in which

the different journals are obtainable (Part IV). The latter is one of the most essential sections of the index, as it enables the reader to locate in London libraries any part required.

The Society for Cultural Relations and the compiler of this index have performed a useful service which will be appreciated by all workers who desire to consult the contemporary medical literature of the USSR.

It is to be regretted that the author has left out certain Russian periodicals which have already been indexed in the *Index Medicus*, since the latter does not provide a guide to their location. The reviewer has also noticed one or two omissions, e.g. *Meditsinskaya Parazitologiya i Parazitarnye Bolezni* (Moscow), of which vols. 14 (1945), 15 (1946) are obtainable at the library of the London School of Hygiene and Tropical Medicine and vol. 16 (1947) at the British Medical Association library.

C. A. Hoare

PARTICULARS OF BOOKS REVIEWED ELSEWHERE IN THIS NUMBER

The numerals in square brackets are the PAGE *numbers of the articles in which these books are reviewed*

[87] Industrial Fluorosis : a Study of the Hazard to Man and Animals near Fort William, Scotland

John N. Agate et al. London : His Majesty's Stationery Office, 1949. (Medical Research Council Memorandum, No. 22.) viii + 131 pages ; 8 plates. 24 × 15 cm. 4s. [£0.2]

(i) Studies of the contamination produced in the Fort William area by fluorine compounds ; (ii) effects of fluorine compounds on animals in the Fort William area ; (iii) clinical, radiological, haematological and biochemical findings in selected groups of individuals from the districts of Fort William and Kinlochleven ; (iv) the dental condition of adults and school-children in the Fort William area ; (v) physical properties of bone in fluorosis ; (vi) summary. Appendix A : the toxicity of fluorine compounds, a review of the literature. Appendix B : a description of analytical methods. References.

[90] Sight, Light and Efficiency

H. C. Weston. London : H. K. Lewis & Co. Ltd., 1949. xiv + 308 pages ; 132 illustrations. 25 × 16 cm. £2 2s. [£2.1]

(i) The sense of sight ; (ii) the causes and symptoms of eyestrain ; (iii) occupational demands upon sight ; (iv) the facilitation of visual tasks ; (v) lighting and visual efficiency ; (vi) incentive luminance and colour ; (vii) testing sight for work ; (viii) the protection of sight at work. Appendix I. Appendix II. Index.

[92] Operative Obstetrics. A Guide to the Difficulties and Complications of Obstetric Practice

J. M. Munro Kerr & J. Chassar Moir. Fifth edition. London : Baillière, Tindall & Cox, 1949. viii + 948 pages ; 390 figures. 25 × 17 cm. £3 3s. [£3.15]

(i) The management of normal labour ; (ii) dystocia from faults in the forces ; (iii) dystocia from faults in the foetus ; (iv) dystocia from faults in the parturient canal ; (v) obstetric operations ; (vi) injuries and accidents to mother and child. Index.

[93] Biochemistry in Relation to Medicine

C. W. Carter & R. H. S. Thompson. London : Longmans, Green & Co., 1949. xi + 442 pages ; 37 illustrations. 22 × 14 cm. £1 5s. [£1.25]

(i) Historical introduction ; (ii) physico-chemical considerations ; (iii) the chemistry of the carbohydrates ; (iv) the chemistry and metabolism of the lipides ; (v) the chemistry of the amino-acids and proteins ; (vi) enzymes ; (vii) biological oxidations ; (viii) haemoglobin and allied pigments ; (ix) electrolytes of the body ; (x) acid-base equilibrium ; (xi) carbohydrate metabolism ; (xii) nutrition and the chemistry of the foodstuffs ; (xiii) vitamins ; (xiv) bile ; (xv) urine ; (xvi) plasma proteins ; (xvii) gastric function ; (xviii) liver function ; (xix) pancreatic function ; (xx) kidney function. Appendix I : identification of substances of biological importance. Appendix II : special techniques. Appendix III : special reagents. Appendix IV : physico-chemical constants. Bibliography. Index.

[99] Opera Selecta

Joannis Evangelistae Purkyně [Purkinje]. Prague : Spolek Českých Lékařů, 1948. (Opera Facultatis Medicae Universitatis Carolinae Pragensis, Tomus I.) 182 pages ; 8 plates. 28 × 19 cm.

(i) Symbolae ad ovi avium historiam ante incubationem. 1825. (ii) Commentatio de examine physiologico organi visus et systematis cutanei. 1823. (iii) Beiträge zur Kenntniss des Sehens in subjectiver Hinsicht. 1819. (iv) De theoria cellulari commentationes tres. (v) Podrobné zprávy o mojích starších i novějších literárních, zvláště přírodnických pracích. Bibliographia.

[100] Lord Lister : his Life and Doctrine

Douglas Guthrie. Edinburgh : E. & S. Livingstone Ltd., 1949. viii + 128 pages ; 21 plates. 23 × 17 cm. 15s. [£0.75]

(i) Surgery before Lister ; (ii) early influences ; (iii) Lister and Syme ; (iv) the antiseptic principle ; (v) the clue and the discovery ; (vi) the return to Edinburgh ; (vii) the mission to London ; (viii) success and honour. Index.

[101] William Withering of Birmingham, M.D., F.R.S., F.L.S.

T. Whitmore Peck & K. Douglas Wilkinson. Bristol : John Wright & Sons Ltd., 1950. viii + 239 pages ; 52 plates. 23 × 15 cm. £1 1s. [£1.05]

(i) Introductions ; (ii) beginnings ; (iii) training ; (iv) the young physician ; (v) an account of the foxglove ; (vi) the general hospital ; (vii) medical practice ; (viii) interests ; (ix) property ; (x) the riots of 1791 ; (xi) tuberculosis. Bibliography. Appendix. Index.

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Shorter Notices

Penicillin and Other Antibiotics

G. W. S. Andrews & J. Miller. London: Todd Publishing Group Ltd., 1949. vi + 160 pages; 4 plates; 7 figures. 19 × 13 cm. 7s. 6d. [£0.375]

This small volume is devoted mainly to penicillin, but gives a brief account of streptomycin. It is symptomatic of the rate of progress in the antibiotic field that chloromycetin and aureomycin are mentioned only in a brief appendix.

The reviewer found it difficult to decide which group of the population the authors mean this volume to reach: perhaps the curious general practitioner who wishes to know more about his tools; perhaps the scientist from another field; perhaps the enquiring layman or the student; certainly not the expert. But how will the general reader, without specialist knowledge, find out the meaning of the technical terms employed by the authors? The style is clear and simple, and the book is easy to read (provided the reader is already familiar with the field), but it is written with the deceptive simplicity of the expert. The authors might well have used a few extra pages to explain some of their technicalities.

The book ranges over a remarkably wide field, from pure structural chemistry to clinical applications, and gives a readable account of the early history of antibiotic research.

T. S. Work

Proceedings of the British Medical Association

British Medical Association. London: Butterworth & Co. Ltd., 1949. xxvi + 468 pages; 56 figures. 25 × 16 cm. £1 5s. [£1.25]

The annual meeting of the British Medical Association affords opportunities for British medical men to read papers on their special subjects. The 1949 meeting was no exception, and those who are seeking for a cross-section of contemporary British medical science will find it in these Proceedings.

The more important papers are published in full, and summaries are provided of others. References are also given, and, though much of the material is of necessity also published elsewhere, the volume will perform a useful function if it carries information about British medical practice and research to places abroad where British medical journals are not easily obtainable or accessible.

It will be seen from the contents that the field covered is very wide, so that it will be difficult for a medical man to pick up this volume without reading something of interest. Many of the subjects on which the greatest number of medical men seek guidance are dealt with at length. In the section on medicine there are complete papers on streptomycin, radioactive substances in clinical medicine, and anticoagulant therapy. The choice of treatment in peptic ulcer is well summarized, and discussion of peptic ulceration from the unusual angle of sociological aspects brings out the information that ulcer incidence is highest in doctors.

Some papers are of special interest because they summarize recent advances, e.g. "Recent advances in knowledge of influenza" by C. H. Andrewes; others, like "Uses and abuses of chemotherapy", reflect varying views on, for example, the use of penicillin. The anatomists and physiologists make their contribution with such papers as "Control of activity in gastro-intestinal tract" and "Factors regulating blood flow in the skin", and there is even an article on "An apparatus to simplify clinical photography"; the last named is of particular interest now that many hospitals and medical schools are setting up their own photographic departments. In addition to the sections on medicine and surgery, every important specialty is represented. Many of the papers, such as Professor Frazer's contribution on fat metabolism and the sprue syndrome, have a wider interest.

F. T.

Biological Actions of Sex Hormones

Harold Burrows. Second edition. Cambridge: University Press, 1949. xiii + 615 pages; figures. 25 × 18 cm. £2 2s. [£2.1]

On reading the 1st edition[1] of Dr Harold Burrows' book some years ago, one was impressed by the industry and accuracy of the author, but at the same time one was a little anxious as to whether this amount of hard work would meet with its just reward in a successful sale of the book. It was difficult to picture clearly to whom the volume would really appeal. For the biochemist and chemist, the volume was not full enough, and to the general biologist the field appeared too restricted.

Fortunately the appearance of the 2nd edition indicates that Dr Burrows was correct in producing his book. Suffice it to say that this work has now been brought up to date and those who possess the 1st edition must surely purchase the 2nd.

Dr Burrows is to be congratulated on the production of a work characterized by thoroughness and accuracy, and also on his perspicuity in perceiving that such a work was really needed.

E. C. Dodds

[1] For review of 1st edition, published in 1945, see *Brit. med. Bull.* 1946, 4, 155

Handbook of Medical Protozoology for Medical Men, Parasitologists and Zoologists

C. A. Hoare. London: Baillière, Tindall & Cox, 1949. xv + 334 pages; 43 figures; 3 plates. 24 × 16 cm. £1 15s. [£1.75]

This is an admirable book. The subject-matter is presented plainly and clearly, and there are many simple and useful diagrams. It covers adequately the author's intention of filling "a gap in the medical curriculum by providing students and practitioners of medicine with all the essential information regarding the protozoa living in man . . ." and of being also of service to Colonial medical officers and zoologists.

It is divided into three Parts: I, General account of the protozoa; II, Systematic account of the protozoa; and III, Diagnostic methods in protozoal infections. The material is deliberately treated didactically and to some extent dogmatically, making for clarity of expression which will be appreciated perhaps more by the student for whom the book was written than by the purist. There is much emphasis on host-parasite relationships, but purely clinical aspects are brought in only where they are necessary to complete the picture. The first Part may appear somewhat too long to many readers, but the second Part is very well done, despite omissions and opinions that might sometimes surprise the more technically trained reader. The third Part, dealing with diagnostic methods, is very clearly presented and will form a valuable asset to any clinical pathological laboratory.

The book is beautifully printed and well set out. It should be very widely read.

B. G. Maegraith

Buchanan's Manual of Anatomy

Edited by *F. Wood Jones*, assisted by *E. L. Patterson, T. E. Barlow, S. Mottershead & F. R. Wilde.* Eighth edition. London: Baillière, Tindall & Cox, 1949. viii + 1616 pages; 49 plates; 847 figures. 23 × 15 cm. £2 5s. [£2.25]

Forty years ago Buchanan's topographical textbook of human anatomy was generally accepted as an authoritative and reliable work by students of anatomy, and its position remains unaltered now that it appears under the editorship of Professor F. Wood Jones, Sir William Collins Professor of Human and Comparative Anatomy at the Royal College of Surgeons of England. The editor, with his collaborators, has thoroughly revised the text of the 7th edition without any alteration in format, and has retained the useful glossary, containing abbreviated biographical notes (from Dobson's *Anatomical eponyms*) on those anatomists whose names are included in the text. The restoration of the original line drawings of James T. Murray, the Edinburgh artist, is an outstanding feature of the 7th and 8th editions; 180 new line drawings have been added, of which 30 have been borrowed from Professor Wood Jones' books, *Structure and function as seen in the foot*, and *Principles of anatomy as seen in the hand.*

H. M. C.

A Manual of Practical Tropical Sanitation

J. Balfour Kirk. Second edition. London: Baillière, Tindall & Cox, 1949. vii + 288 pages; 46 figures. 20 × 13 cm. 10s. 6d. [£0.525]

Dr Balfour Kirk, formerly Director of the Medical and Health Department of Mauritius, has now brought up to date this manual, originally published in 1937, for the use of those following a course of instruction in the work of sanitary inspectors in the tropics. Technical terms are defined and plain language used so that the book may also prove valuable to those faced with the health problems of labour forces in mines and factories, and on estates where technical aid is not readily available. From a clear exposition of the channels of infection, and methods of prevention of the most prevalent tropical diseases, the author passes to disinfection, hygiene of food and drink, and the main branches of sanitary inspection technique.

H. M. C.

Practical Public Health Problems

William Savage. Second edition. London: J. & A. Churchill Ltd., 1949. vii + 197 pages. 22 × 14 cm. 14s. [£0.7]

Sir William's slim volume has always had a place of its own because it deals with selected important public health problems of special interest to the doctor and medical student. The latter, stunned by the wealth of information and detail contained in the large, standard textbooks on public health, will be glad to turn to these pages written by a medical officer of health (and, be it noted, an examiner) of wide experience, with an enthusiasm for his subject.

It is not surprising that the chapter, "The investigation of enteric outbreaks", has been added to the present edition "in response to a number of requests" for it is a subject that has attracted a good deal of interest in recent years, and Sir William's readable account is not easily paralleled elsewhere. Attention is also directed to the chapter, "Hygienic food control", which replaces the one in the previous edition on the Food and Drugs Act, 1938.

The section on ice-cream is very up to date and includes references to the provisions of the recent *Ice Cream (Heat Treatment, etc.) Regulations, 1947*. The two opening chapters on water supplies, with references to recent legislation, are also of special interest.

As it is obvious that the author has been at great pains to revise his work, one can only conclude that the *Milk and Dairies Regulations, 1949* were published too late to receive mention. Similarly the *Milk (Special Designations) Order, 1936* quoted on page 86 has been superseded by the *Milk (Special Designation) (Raw Milk) Regulations, 1949*. In the section on air infection and disinfection (page 190) it would have been helpful to have included a direct reference to the Medical Research Council's important report on the subject. Hospital librarians and all who have the care of circulating libraries should read the author's pithy remarks on book disinfection on pages 192–193.

In conclusion, this is an eminently readable book for all public health workers, medical men interested in public health, and students.

F. T.

Rehabilitation, Re-education and Remedial Exercises

Olive F. Guthrie Smith. Second edition. London : Baillière, Tindall & Cox, 1949. xii + 456 pages ; 283 figures. 23 × 16 cm. £1 5s. [£1.25]

Mrs Guthrie Smith, formerly principal of the Swedish Institute and of the Physical Exercise Department, St Mary's Hospital, London, here includes new material of interest to all physiotherapists. She describes and gives illustrations of a new mobile apparatus which she herself designed for bed-fast rheumatic and geriatric patients, and in an appendix she gives a useful chart of the postural drainage positions for chest conditions. Other contributions by specialists now introduced include chapters on arthroplasty of the hip joint, arthritis of the hip, and rehabilitation after injuries to the spinal cord and cauda equina. As in the 1st edition, there is an authoritative account of Mrs Guthrie Smith's original work on "suspension" methods which are now taught and practised in many countries of the world, including America, where suspension apparatus is installed in many Veterans' Hospitals. Minor corrections and alterations bring this authoritative textbook up to date.

H. M. C.

The Radcliffe Infirmary Handbook

[Edited by *Sidney Truelove & A. M. Cooke.*] Oxford : University Press, 1949. 150 pages. 19 × 13 cm. 7s. 6d. [£0.375]

Dr John Radcliffe (1650–1714) is famous in medical history for having forfeited the regard of William III by dismissing the king's swollen ankles and emaciated body with the remark "Why truly, I would not have your Majesty's legs for your three kingdoms." But Radcliffe's claim to fame rests on surer foundations, namely the Infirmary, Library, Observatory and Travelling Scholarships which bear his name, and which his various bequests made possible. It is fitting that the Institute for Medical Research, named after that other munificent benefactor to Oxford, Lord Nuffield, should be housed in the Radcliffe Observatory, and that Nuffield Professors should be in the Radcliffe Infirmary.

Radcliffe himself had few books, and claimed that a few phials, a skeleton, and a herbal constituted his library, but he was an eminently practical physician and would have wholly approved of the idea behind the present handbook. It tells the house officers for whom it is primarily intended "How to do things, where to get things, who is who and what is what."

Some of this information is of purely local interest—By-law 7, for example, which deals with guests ; but By-law 11 "All House Officers are required to join a Medical Protection Society" can be said to give good, sound advice to any newly qualified medical man.

The bulk of the book is packed with essential facts of wide application, and with useful information not always easily obtainable elsewhere. The chapter on note-taking is a model of the clarity that pervades the whole work, and the section of it entitled "Instructions to house surgeons to the neurosurgical department" affords an example of the type of information often needed but sought in vain. Others besides house officers will be glad to have by them the instructions for carrying out practical procedures given in the volume, for these include red-cell counts, haemoglobin estimation, and other routine tests which modern clinical pathology brings to the aid of medical diagnosis. As the latter are grouped under the heading "Investigations to be performed by house officers when the laboratory is closed", a subject index would greatly add to the value of this section alone, and certainly to the *Handbook* as a work of reference.

One could continue to single out sections for favourable comment, but a word must be said for "Notes on the management of head injuries" because expert guidance is not so easily available elsewhere in such concise form.

F. T.

Sobre la Pretendida Influencia de la Tensión Intratorácica y sus Variaciones, en la Génesis y Evolución de las Cavernas y el Enfisema Pulmonares

N. Gonzalez de Vega y Soto. Madrid : Publicaciones del Patronato Nacional Antituberculoso, 1949. 100 pages ; 36 figures. 25 × 17 cm.

This monograph contains a most detailed review of the theories so far put forward on cavity formation and cavity closure. The author refutes the general belief that "ballooning" of cavities is the direct consequence of bronchial valve action. In his opinion the entrance of air into the lung is a passive phenomenon due to the decreased pressure inside the thorax, produced by its dilatation. There is no such thing as one pressure inside the cavity and another in the surrounding parenchyma. During coughing the pressure in the cavity increases and so does the pressure in the tissues round the cavity. The mechanical theories of Monaldi and Coryllos do not explain this and we must acknowledge that there are other factors, such as the active contraction and dilatation of the lung propounded long ago by Bronkhorst and Dijkstra and more recently by Parodi, Xalabarder and others.

A. J. Coello

Diseases of the Nervous System : Described for Practitioners and Students

F. M. R. Walshe. Sixth edition. Edinburgh : E. & S. Livingstone Ltd., 1949. xvi + 359 pages ; 60 figures. 25 × 16 cm. 17s. 6d. [£0.875]

Textbooks of neurology are generally of such formidable dimensions that they can be appreciated only by the specialist. Here, however, in the space of some 350 pages, is presented an easily read story which has already in its previous editions been widely adopted by both student and practitioner as the neurological textbook suitable for their requirements. It is indeed fortunate that Dr Walshe has found time to apply his well-known mastery of words and clarity of thought to this task. Not that this textbook is beyond criticism, for some subjects are dealt with in a rather old-fashioned way, but as an introduction to the subject of neurology it is quite the best book of its kind known to the reviewer.

W. Ritchie Russell

New Editions

Pye's Surgical Handicraft. A Manual of Surgical Manipulations, Minor Surgery, and Other Matters Connected with the Work of Surgical Dressers, House Surgeons and Practitioners

Edited by *Hamilton Bailey.* Sixteenth edition. Bristol : John Wright & Sons Ltd., 1950. xii + 724 pages ; 830 figures. 22 × 15 cm. £1 5s. [£1.25]

This is the 16th edition of one of the textbooks which every doctor has used. There is no major addition to the contents but the editor, appreciating the increasing popularity of this famous publication in the USA, has thought it appropriate to include some American contributions in this edition. The previous edition was reviewed in Shorter Notices in *British Medical Bulletin*, 1947, Vol. 5, p. 100.

Surgery for Nurses

Hamilton Bailey & R. J. McNeill Love. Seventh edition. London : H. K. Lewis Ltd., & Co. 1950. vii + 551 pages ; 555 illustrations. 22 × 14 cm. £1 1s. [£1.05]

This edition has been completely revised. Besides being a practical handbook for nurses it states the principles of surgery which they should know. Most chapters end with questions quoted from the Final State Examination of the General Nursing Council.

Combined Textbook of Obstetrics and Gynaecology for Students and Practitioners

Edited by *Dugald Baird.* Fifth edition. Edinburgh : E. & S. Livingstone Ltd., 1950. xii + 1411 pages ; 594 illustrations. 25 × 16 cm. £3 10s. [£3.5]

The author, in the preface to this edition, says that the emphasis in obstetrics and gynaecology "is now increasingly on the preventive and physiologica approach". The text has therefore been amended to meet changing needs.

Special attention is given to the physiology of pregnancy and there are new chapters on stillbirth, infant mortality and psychological factors.

The Practice of Orthoptics

G. H. Giles. Second edition. London: Hammond, Hammond & Co. Ltd., 1949. 407 pages; 72 illustrations. 22 × 14 cm. £1 10s. [£1.5]

This book was first published in 1943. The 2nd edition has many alterations and several new sections, including one on the uses of contact lenses in strabismus and heterophoria. The 3rd impression of the 1st edition, published in 1947, was reviewed in *British Medical Bulletin*, 1949, Vol. 6, p. 105.

Medical Jurisprudence and Toxicology

John Glaister. Ninth edition. Edinburgh: E. & S. Livingstone Ltd., 1950. xi + 755 pages; 234 illustrations. 22 × 14 cm. £1 15s. [£1.75]

This 9th edition of Glaister helps to maintain the pre-eminence of the Scottish school of forensic medicine. A chapter on the effects of the atomic bomb replaces that on war gases, and new material is included on such subjects as the liability of hospitals and nursing homes, finger-prints, medico-legal aspects of artificial insemination, and Rh subtypes.

Gray's Anatomy: Descriptive and Applied

Edited by *T. B. Johnston & J. Whillis.* Thirtieth edition. London: Longmans, Green & Co., 1949. xix + 1533 pages; 1333 illustrations. 26 × 17 cm. £4 4s. [£4.2]

The 30th edition of this work has been carefully revised, substantial portions of the text have been rewritten, and many of the original figures have been replaced. Responsibility for the individual sections remains unchanged in this edition, with the exception that Professor Francis Davis has undertaken the section dealing with the respiratory system in addition to that on the digestive system. The editors have endeavoured to reduce the bulk of this large volume by avoiding undue repetition and, despite the addition of much new material, a saving of more than 60 pages has been obtained.

The Diabetic Life: its Control by Diet and Insulin. A Concise Practical Manual for Practitioners and Patients

R. D. Lawrence. Fourteenth edition. London: J. & A. Churchill Ltd., 1950. xi + 238 pages; 18 illustrations. 21 × 14 cm. 10s. 6d. [£0.525]

The author has brought the 14th edition of this well-known book up to date, in the light of new knowledge, but still keeps to his object in providing a simple and practical guide for the management of diabetes. The 13th edition was reviewed in *British Medical Bulletin*, 1944, Vol. 2, p. 90.

Green's Manual of Pathology

Revised by *H. W. C. Vines.* Seventeenth edition. London: Baillière, Tindall & Cox, 1949. viii + 1200 pages; 730 illustrations. 24 × 16 cm. £2 2s. [£2.1]

In his preface to this edition Dr Vines discusses the gradual disappearance of the rigid border-line between physiology and pathology in experimental work. He says, too, that the success of new agents such as the arsenobenzenes, the sulphonamides and the antibiotics are modifying the pathological lesions of many forms of infection; and that, sooner or later, a new type of textbook with a broader outlook will have to be written. Meanwhile the text of this book has been added to and the number of new illustrations and colour plates has been increased. The subjects are described in two main sections: general pathology and systematic pathology.

Books Received

February 1950—June 1950

Reviews of many of these books appear in this number of the Bulletin or will appear in future numbers

Abse, D. W. *The diagnosis of hysteria.* 1950. Wright (Bristol), 8s. 6d. [£0.425]

Actualités pharmacologiques. Publiées sous le direction de René Hazard. Deuxième série par M. Chambon, J. Cheymol, Ph. Decourt, C. Huriez, L. Launoy, M. Macheboeuf, P. Mentzer, M. Perrault & A. Simonart. 1950. Masson (Paris), 850 fr.

Almeyda, J. *Major symptoms in clinical medicine.* Vol. 1. 1950. Kimpton (London), £1 5s. [£1.25]

Baclesse, F. *Carcinoma of the larynx. With a statistical report on cases treated with X rays only.* By R. W. Gunderson. (*British Journal of Radiology*, Supplement No. 3.) 1949. British Institute of Radiology (London), £1 5s. [£1.25]

Bailey, H. *Emergency surgery.* Part III. 16th ed. 1950. Wright (Bristol), £1 1s. [£1.05]

Bailey, H., editor. *Pye's surgical handicraft. A manual of surgical manipulations, minor surgery, and other matters connected with the work of surgical dressers, house surgeons and practitioners.* 16th ed. 1950. Wright (Bristol), £1 5s. [£1.25]

Bailey, H. & Love, R. J. M. *Surgery for nurses.* 7th ed. 1950. Lewis (London), £1 1s. [£1.05]

Baird, D., editor. *Combined textbook of obstetrics and gynaecology: for students and practitioners.* 5th ed. 1950. Livingstone (Edinburgh), £3 10s. [£3.5]

Barbàra, M. & Puppo, B. L. *Studii di stomatologia costituzionalistica.* (Collana di monografie dell' *Archivio* "*E. Maragliano*" *di Patologia e Clinica*, No. 1.) [no date] Istituto di Patologia Medica dell' Università (Genoa), 500 lire

Bayliss, R. I. S. *Practical procedures in clinical medicine.* 1950. Churchill (London), £1 5s. [£1.25]

Bell, A. C. H. *A pocket obstetrics.* 2nd ed. 1950. Churchill (London), 7s. 6d. [£0.375]

Bigger, J. W. *Handbook of bacteriology, for students and practitioners of medicine.* 6th ed. 1949. Baillière (London), £1

Biochemical Society. *Biochemical aspects of genetics.* (Biochemical Society Symposia, No. 4.) Organized and edited by R. T. Williams. 1950. University Press (Cambridge), 6s. [£0.3]

Bisset, K. A. *The cytology and life-history of bacteria.* 1950. Livingstone (Edinburgh), 18s. 6d. [£0.925]

Blanc, F. & Siguier, F. *L'amibiase: étude clinique et thérapeutique.* 1950. L'Expansion Scientifique Française (Paris)

Böhmig, R. *Form- und Wachstumsgesetze drüsenbildender Karzinome.* 1950. Thieme (Stuttgart), 3.35 Mk.

Bolton, E. R. & Revis, C. *Oils, fats and fatty foods: their practical examination.* 3rd ed., revised by K. A. Williams. 1950. Churchill (London), £3 3s. [£3.15]

Boyce, F. F. *Acute appendicitis and its complications.* 1949. Oxford University Press (New York); Geoffrey Cumberlege (London), £3 10s. [£3.5]

British Medical Association. *Proceedings of the Annual Meeting, 1949.* 1950. Butterworth (London), £1 5s. [£1.25]

British Rheumatic Association. *Second annual report, 1948–1949.* [1950] British Rheumatic Association (London)

Browne, F. J. *Postgraduate obstetrics and gynaecology, 1950.* 1950. Butterworth (London), £2 10s. [£2.5]

Bücker, J. *Gastritis, Ulkus und Karzinom.* 1950. Thieme (Stuttgart), 11.50 Mk.

Cade, S. *Malignant disease and its treatment by radium.* Vol. 3. 2nd ed. 1950. Wright (Bristol), £2 12s. 6d. [£2.625]

Central Council for Health Education. *Report, 1948–9.* [1950] Central Council for Health Education (London)

Children's Reception Centre, Mersham, Kent. *Interim Report 1948.* 1949. Caldecott Community (Kent)

Clark, W. E. Le G. *History of the primates. An introduction to the study of fossil man.* 1949. Printed by order of the Trustees of the British Museum (London), 2s. 6d. [£0.125]

Clark-Kennedy, A. E. *Lectures on medicine to nurses.* 1950. Livingstone (Edinburgh), 15s. 6d. [£0.775]

Clements, F. W. *Infant nutrition: its physiological basis.* 1949. Wright (Bristol), £1 1s. [£1.05]

Cobb, W. A., Hill, D., Greville, G. D., Walter, W. G., Heppenstall, M. E. & Whitteridge, D. *Electroencephalography. A symposium on its various aspects.* Edited by Denis Hill & Geoffrey Parr. 1950. Macdonald (London), £3 18s. [£3.9]

Collins, D. G. *The pathology of articular and spinal diseases.* 1949. Arnold (London), £1 15s. [£1.75]

Committee of Privy Council for Medical Research. *Report of the Medical Research Council for the years 1945–1948.* (Cmd. 7846.) 1949. His Majesty's Stationery Office (London), 5s. [£0.25]

Corwin, E. H. L., editor. *Ecology of health. The New York Academy of Medicine Institute on Public Health, 1947.* 1949. Commonwealth Fund (New York); Geoffrey Cumberlege, Oxford University Press (London), £1

Crohn, B. B. *Regional ileitis.* 1949. Staples Press (London), £1 10s. [£1.5]

Curtis-Bennett, N. *The food of the people: being the history of industrial feeding.* 1949. Faber & Faber (London), 16s. [£0.8]

Cyriax, J. *Osteopathy and manipulation.* 1949. Crosby Lockwood (London), 6s. [£0.3]

Dennig, H., editor. *Lehrbuch der inneren Medizin.* Vol. 1. 1950. Thieme (Stuttgart), 29.70 Mk.

Domagk, G. *Chemotherapie der Tuberkulose mit den Thiosemikarbazonen.* 1950. Thieme (Stuttgart), 60 Mk.

Doyle, L. *Handbook of obstetrics and diagnostic gynecology.* 1950. University Medical Publishers (Palo Alto, California), 14s. [£0.7]

Family Planning Association. *Conference on infertility 1948.* [1950] Family Planning Association (London), 10s. 6d. [£0.525]

Findlay, G. M. *Recent advances in chemotherapy.* Vol. 1. 3rd ed. 1950. Churchill (London), £1 16s. [£1.8]

Fliess, R., editor. *The psycho-analytic reader. An anthology of essential papers with critical introductions.* (The International Psycho-Analytical Library, No. 38.) 1950. Hogarth Press & Institute of Psycho-Analysis (London), 18s. [£0.9]

Forsythe, S. M. *The story of bovine tuberculosis.* 1949. Oak Tree Books (London), 10s. 6d. [£0.525]

Francis, C. *Asthma.* 1950. Heinemann (London), 5s. [£0.25]

BOOKS RECEIVED

Franco, B. B. *Tuberculosis. Estudio de la lucha contra esta enfermedad en España (1919–49).* 1950. Patronato Nacional Antituberculoso (Madrid)

Freud, S. *An outline of psycho-analysis.* (The International Psycho-Analytical Library, No. 35.) 1949. Hogarth Press & Institute of Psycho-Analysis (London), 8s. 6d. [£0.425]

Freud, S. *Collected papers. Volume V: Miscellaneous papers, 1888–1938.* Edited by James Strachey. (The International Psycho-Analytical Library, No. 37.) 1950. Hogarth Press & Institute of Psycho-Analysis (London), £1 5s. [£1.25]

Fulton, J. F. *Physiology of the nervous system.* 3rd ed. 1949. Oxford University Press (New York); Geoffrey Cumberlege (London), £3 15s. [£3.75]

General Register Office. *The Registrar General's estimates of the population of England and Wales. Populations of each administrative area at 30th June, 1949.* 1950. His Majesty's Stationery Office (London), 4d. [£0.0165]

Gibbens, J. *The care of children from one to five.* 4th ed. 1950. Churchill (London), 5s. [£0.25]

Gillison, M. *A histology of the body tissues, with a consideration of their functions.* 1950. Livingstone (Edinburgh), 15s. [£0.75]

Glaister, J. *Medical jurisprudence and toxicology.* 9th ed. 1950. Livingstone (Edinburgh), £1 15s. [£1.75]

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Films

Techniques in Plastic Surgery

made at plastic surgery units of Ministry of Health and Ministry of Pensions, 1949 ; owned by the British Council ; technical adviser, Stephen Ackroyd ; directed by Alistair Scobie ; produced by Gaumont British Instructional Ltd. ; available in 16 mm. only ; kodachrome sound versions in English, French, Spanish

Part 1 : Primary repair and secondary suture ; 560 feet [171 m.] ; 15 minutes
Part 2 : Free grafts ; 1,242 feet [379 m.] ; 35 minutes
Part 3 : Local flaps ; 625 feet [191 m.] ; 18 minutes
Part 4 : Direct flaps ; 498 feet [152 m.] ; 14 minutes
Part 5 : Tubed pedicle flaps ; 758 feet [231 m.] ; 21 minutes
Part 6 : Chip bone grafting ; 526 feet [160 m.] ; 14 minutes

This series of six films provides a comprehensive survey of the basic operative techniques employed at various plastic surgery centres in this country. The technical details of many of these reconstructive procedures are not easily dealt with in written descriptions, and so this branch of surgery lends itself particularly to the medium of the film, a point which is well borne out in the series under review, in which the various operations are clearly demonstrated and should be easily understood by those with little special knowledge of the subject.

Primary Repair and Secondary Suture

The first film deals with the principles of wound repair, illustrating the technique of accurate suturing and the avoidance of excessive trauma to the tissues. After direct suture of part of the defect (a gun-shot wound of the face), the remainder is closed by a rotation flap, complete wound cover without tension thus being obtained. A case of secondary repair is shown in which, four months after the original injury, multiple facial scars are excised and tension on the eyelids relieved.

Free Grafts

The longest film is concerned with the methods of cutting free skin grafts and provides several examples of their application. The Blair knife and the dermatome are demonstrated, the value of the latter instrument in obtaining uniform grafts of any desired thickness being particularly stressed. Split skin grafts are shown providing epithelial cover in a case of burns, and in a case of extensive skin avulsion of the buttocks and sacral region where primary skin replacement had been delayed owing to the poor general condition of the patient. The point is made that thin skin grafts are better able to withstand infection, and their application to a granulating surface in the form of " postage stamps " is shown. It was noticed that thrombin was used for graft fixation in some of these cases, a refinement of technique which is perhaps not employed as frequently in most centres nowadays as in recent years. A further example of the use of the Thiersch graft is in the operation of buccal inlay, the details of which are well presented. The good cosmetic appearance of a successful full thickness graft is apparent in its use in the repair of a forehead defect. Its functional value is illustrated by the replacement of scar tissue on the flexor aspect of thumb and fifth finger in a case of burns of the hand. The skin of the flank is regarded as a good donor site for Wolfe grafts to the hand as it is thick and elastic and the secondary defect is easily closed. An example of how both cosmetic and functional requirements can be met is provided by the post-auricular Wolfe graft to the lower eyelid in a case of ectropion following burns.

Local Flaps

In the film dealing with local flaps we are shown a typical Z-plastic operation for the relief of tension due to a vertical scar in the neck. Other examples under this heading include a small forehead flap to replace a defect below the lower eyelid, a double pedicle bridge flap from the forehead to the chin, and a forehead flap rhinoplasty. A scalp flap is shown being rotated to cover a forehead defect, and the extra rotation produced by a judicious back-cut is well demonstrated. A short sequence dealing with the art of undermining would have been appreciated as it is such an essential feature of the plastic surgeon's technique.

Direct Flaps

Direct flaps are used in the transfer of tissue from a distance when donor and recipient sites can be approximated. A good example is the cross-leg flap which is here employed in a leg injury with some bony loss of the tibia. It is emphasized that bone grafting should not be carried out in such a case until good skin cover has first been provided. The statement that *all* cross-leg flaps should be delayed may not meet with the universal approval of surgeons experienced in this field. An interesting variation in technique is the grafting of the donor site at the first stage, the graft then being buried under the delayed flap. It is pointed out, however, that infection is prone to occur and that the method is not commonly employed. Plaster of Paris fixation is used unless the legs are parallel, when elastic strapping may be preferred. The other example of this type of flap is the replacement of scar tissue in the elbow region by an abdominal flap which is so planned that the joining scar lies on the lateral aspect of the joint where least movement occurs. Raw surfaces are avoided in this as in other similar operations by the raising of a return flap of scar tissue which is sutured to the base of the pedicle.

Tubed Pedicle Flaps

The fifth film is devoted to the use of the tubed pedicle flap, and its value is stressed as a means of transferring skin from any part of the body without running the risk of infection of exposed surfaces. The first case shown is a gun-shot wound of the mandible with loss of soft tissue and bone. An acromiothoracic tubed pedicle is raised and the technique is shown in detail. The four-point stitch closing the triangular defect at each end is demonstrated very clearly, and the correct application of dressings so as to avoid pressure on the pedicle is also included. After an interval of three weeks the lower end is detached, opened out, and let into the recipient site, a small return flap being raised to avoid any raw surface. Elastic strapping is used to prevent undue tension on the new attachment. The final stage shows the division of the lower end, untubing of the flap, and its suture into position. The other example is a case of compound fracture of the tibia in which an abdominal tubed pedicle is transferred in several stages, the wrist being used as an intermediate carrier. Owing to the limited flexion of the affected limb the pedicle has first to be transferred to the opposite leg, so that five stages are required before the procedure is completed. The point is made that, as the scar must be left behind at each stage, it is necessary to plan the original flap a little larger than will ultimately be required.

Chip Bone Grafting

The final film presents the technique of chip bone grafting. The readiness with which cancellous chips acquire a blood supply and become rapidly consolidated, and their value in building up contour, is illustrated in two cases. The first is a mandibular reconstruction in which a gap of two inches between the fragments is filled with bone chips. The iliac crest is exposed, a portion of cancellous bone removed and cut up into suitably sized chips. The mandibular fragments are exposed in a subperiosteal plane and the bone ends freshened. Fixation is obtained by a pin in the posterior fragment which is connected by a rod (insulated so as to prevent ionization) to cap splints on the teeth. A larger portion of cancellous bone is first placed across the gap and the chips are then packed in on top of it. Fixation is removed after four weeks and normal jaw function is allowed, somewhat unexpectedly, after that time. The other example is the restoration of bony contour following the loss of a large part of the frontal bone. The margins of the defect are exposed by careful dissection, the local injection of saline and adrenaline solution being used to assist in finding the correct plane of cleavage. A single bony strip is used to define the supra-orbital ridge and the rest of the gap filled with chips which are carefully placed to avoid irregularity. An external mould and pressure dressings are applied at the end of the operation.

These well-produced films, in a total running-time of approximately two hours, succeed in covering many aspects of the field of plastic surgery. The techniques employed and the method of approach to the surgical problems presented can be said to be representative of the current procedures in the major British centres of plastic surgery. Such an authoritative presentation of the subject and the clarity with which the various operations are depicted ensures that this series is of great value for teaching purposes. On the technical side little fault can be found, and the direction and editing are of a very high order. The sequences are well chosen and always to the point, and we are spared, for example, the irritating by-play with artery forceps which ruins the tempo of so many surgical films. Colour is used throughout and uniform lighting and exposure are maintained with very few lapses. The well-written commentary is admirably delivered and succeeds in being unobtrusive while yet adding greatly to the value of the presentation.

A. J. Evans

Before and After the Baby

made in Glasgow at the Women's Hospital, Rotten Row, 1948 ; devised by Margaret Morris in collaboration with M. Randall ; produced by Movement Therapy Films ; obtainable from Movement Therapy Films, 299 West George Street, Glasgow, C. 2 ; available in 16 mm. silent, 800 feet [244 m.] ; black and white ; 30 minutes

The first half of this film, although interesting and instructive in many ways, is perhaps already a little out of date. Antenatal exercises, as such, are now widely recognized to play only a part in the general education of the expectant mother. Training for child-birth should co-ordinate simple instruction in the physiology of pregnancy, the events of labour, and the preparation for lactation. Exercises can be used as a focal point for this teaching and explanation, and are also of value in making the patient appreciate the state of contraction and relaxation of the various muscles involved in labour. She should learn from the exercises how and when to relax, and how and when to use the muscles of expulsion. With this wide background she may approach her confinement with confidence and interest.

The individual exercises in the film are accompanied by brief comments on their purpose, but the exact application to the coming labour is not made clear. One must admire the graceful performances of the actresses, while wondering whether the purpose of the performance would be apparent to the audience for whom it is designed—patients, midwives, and medical students.

The second half of the film, which deals with postnatal exercises, is much more practical and realistic. Instead of being demonstrated by one lady against draped curtains, and later by a row of solemn patients sitting on hard chairs, the postnatal exercises are performed by cheerful mothers on their beds in a ward. The purpose of the manoeuvres, to re-educate stretched muscles and improve the patient's general sense of well-being, is well and clearly shown. Two patients are followed to their own homes and, after delightful shots of the new babies, their proud and very healthy-looking mothers show that they are continuing their exercises until they are really fit once more.

This film should be shown only with a suitable commentator, such as a doctor, physiotherapist, or midwife, to explain the part of exercises in the whole training scheme, and to describe rather more fully the purpose of each one. Used in this way it could be of considerable help to the audiences for whom it was devised.

Aileen Dickens

Control of Infection in Surgical Dressings

made for Imperial Chemical Industries Ltd., at the Birmingham Accident Hospital, 1947–49 ; obtainable from Imperial Chemical Industries Ltd. ; technical adviser, Dr Leonard Colebrook ; available in 16 mm. sound ; kodachrome

Part 1 : Sources and channels of infection ; 650 feet [198 m.] ; 18 minutes
Part 2 : Dressing technique for small wounds ; 750 feet [229 m.] ; 18 minutes
Part 3 : Dressing technique for large wounds, particularly burns ; 910 feet [277 m.] 28 minutes

This film shows, in three parts, the latest methods for control of infection in surgical dressings. The exposition is clear but there is too much repetition of material from one part to another. This repetition might be useful if the films are seen separately but seems unnecessary when the three parts are shown together. Part one, " Sources and Channels of Infection," is an introduction to parts two and three on " Dressing Technique for Small Wounds " and " Dressing Technique for Large Wounds, Particularly Burns." It opens with a series of diagrams and demonstrations of the losses of man-power caused by injuries, and stresses in particular the unnecessary additional loss of man-hours due to septic infection. Emphasis is laid on two particular channels of infection—self-infection in which the patient's wound may become infected from his or her own body, and cross-infection in which the infection comes from some outside source such as another patient, nurse, or doctor.

Much attention is given to air-borne infection and proof of this method of infection is given by a demonstration of the " slit-sampler ", which is described in detail.

The scattering of infected particles during the removal of a dressing and during bed-making in a ward is shown. The precautions used by the bacteriologist in order to avoid the transfer of unwanted bacteria are shown to form the basis on which dressers carry out their technique of surgical dressings, a strict no-touch technique being advocated. Part one ends with a scene in which a nurse deliberately enacts the kind of mistakes commonly made in surgical dressing. Part two, " Dressing Technique for Small Wounds", begins with a diagram showing the sources of self- and cross-infections. This part deals with the treatment of relatively small wounds where the risk of air-borne infection is not very great, the emphasis being placed on the risk of contact infections which can be prevented by a good aseptic dressing technique. This is first demonstrated by showing the technique for one nurse in a factory surgery, followed by the technique adopted for a team of nurses in a hospital out-patients' department. A model is used to show the lay-out of the Birmingham Accident Hospital Dressing

Station. The film, beginning in the out-patients' waiting-room, follows the patient through the whole sequence of events when he passes through the inspection room and one of the dressing-rooms for treatment. Every stage from the removal of the bandages, the no-touch technique for the removal of the inner dressings, disposal of used material, inspection of the wound and method of prescribing treatment is shown. The patient is then followed into the treatment room where treatment is followed stage by stage. Part three, "Dressing Techniques for Large Wounds, Particularly Burns", is the longest part and deals particularly with problems of air-borne infection. Ventilation systems are shown in great detail and a slit-sampler is used to demonstrate the purity of the air in the dressing-station compared to that in a normal hospital ward. The film continues with shots of the transfer of a patient from a ward to the dressing-room and shows the treatment and final bandaging of a wounded leg. It concludes with a demonstration of the results obtained by these methods.

J. G.

Industrial Dermatitis

produced by Crown Film Unit for the Ministry of Labour, 1950 ; introduced by Dr Sybil Horner ; obtainable from Central Film Library, Imperial Institute, London ; available in 35 and 16 mm. sound, 1,385 feet [422.2 m.] and 554 feet [169 m.] respectively ; black and white ; 16 minutes

This film is built round a simple story. The manager of a paint factory, worried by the drop in production, traces the cause to the number of men sick with industrial dermatitis. A doctor is engaged to work full time in the factory. He is an immediate success. The incidence of dermatitis falls by two-thirds. But a new problem arises. Two "barrack-room lawyers", who do not carry out his instructions, show no improvement. Faith in the preventive methods introduced is shaken and morale in the factory is low. The doctor visits the two men's wives and with their co-operation cures the men. The film ends with another victory for the doctor, this time over a case of dermatitis in a worker who takes all precautions but is, unfortunately, prone to the disease. The works manager and the doctor co-operate in finding him other work, and the closing scenes show them congratulating each other, and the worker smiling happily.

The simplicity of this film should make it especially suitable for showing to factory workers and their employers. It should also help any factory doctor convince his charges how often industrial dermatitis is preventable.

J. G.

Five Surgical Operations

made in the Department of Surgery, Guy's Hospital, London, 1948–49 ; produced by Kinocrat Films Ltd., for Guy's Hospital ; obtainable from Kinocrat Films Ltd., Kinocrat House, Cromwell Road, London, S.W. 7 ; available in 16 mm. silent ; kodachrome

(i) Radical mastectomy ; 476 feet [147 m.] ; 20 minutes
(ii) Thyroidectomy ; 380 feet [116 m.] ; 15 minutes
(iii) Haemorrhoidectomy ; 276 feet [84 m.] ; 11½ minutes
(iv) Fistula in ano and anal fissure ; 330 feet [101 m.] ; 14 minutes
(v) Repair of inguinal hernia ; 550 feet [168 m.] ; 24 minutes

These films show standard techniques for five surgical operations. There is little to say about them except that they are very well made, with no unnecessary delays in description or demonstration. The colour and clarity of the operating fields are always excellent. The films should be useful introductions for those about to watch the operations performed in real life.

J. G.

Thiopentone Sodium and its Use in Intravenous Anaesthesia

made with the co-operation of the Department of Anaesthetics, Westminster Hospital, London, 1948 ; produced by National Interest Picture Productions Ltd., for May & Baker Ltd. ; obtainable from May & Baker Ltd., Dagenham ; available in 16 and 35 mm. sound, 1,368 feet [417 m.] and 3,420 feet [1042 m.] respectively ; black and white ; 38 minutes

This film is divided into three distinct sections, namely, chemistry and manufacture, pharmacology, and clinical use of thiopentone sodium. The first section seems too long, chiefly because of the time taken up on the screen by showing many formulae. The second and third sections are more interesting. The pharmacology of thiopentone sodium is shown, emphasis being laid on the depressant effect which the drug has on the central nervous system ; there are also shots of experimental work on the respiration and circulation of laboratory animals. The clinical section covers the main points of pentothal anaesthesia, including, for example, the effects and treatment of accidental intra-arterial injection and the adjuvant use of *d*-tubocurarine.

This film could be an excellent aid for teaching purposes, not only for medical students, but also for nurses and possibly pharmacists.

J. G.

Insulin

made by Wellcome Film Unit, for Burroughs Wellcome Ltd., 1949 ; technical adviser, Dr H. Stewart ; produced by Wellcome Film Unit ; obtainable from Burroughs Wellcome Ltd. ; available in 16 mm. sound, 800 feet [244 m.] ; black and white ; 21 minutes

This is a well-made little film of general interest. There is no new material in it which would be important for insulin users to know. The best audience for this film would be one of diabetics, who should gain even more confidence in insulin after seeing the thoroughness with which it is produced.

J. G.

The Undefeated

produced by World Wide Pictures, 1950 ; sponsored by the Central Office of Information for the Ministry of Pensions ; distributed by Central Film Library, Imperial Institute, London ; available in 35 and 16 mm. sound, 3,168 feet [966 m.] and 1,267 feet [386 m.] respectively ; black and white ; 35 minutes

This film is the story of Joe Anderson, a glider pilot, who loses both legs as a result of a crash landing in north-west Europe during the 1939–45 war. It shows his gradual rehabilitation to civilian life after months spent at Roehampton Hospital learning to use his artificial limbs and to adjust himself to a new and hopeful outlook on the future. There is also a dramatic sequence, showing how he manages to regain the power of speech, lost as a result of his feeling of guilt about the glider accident and the death of a fellow soldier. The film ends with Joe beginning a career as a welfare officer at the Ministry of Pensions.

This is an excellent and moving film. It shows clearly how important it is for the maimed to work hard to overcome their disabilities and how their morale can be kept up in this way as well as by the encouragement and society of others similarly afflicted. Great stress is laid on the part played by Ministry of Pensions' officers in helping these men to return to a full life. Apart from the battle scenes the action takes place chiefly in the hospital and in the Ministry offices. The leading parts are played and spoken by professional actors. This film could be shown to any type of adult audience as its theme is as much a social as a medical problem.

J. G.

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